CLAIMS

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

isolating a population of NKT-like cells from the subject or from a sample derived from the subject;

wherein the glucocorticoid is dexamethasone or betamethasone; and

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 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.

5. The use according to claim 1, wherein the glucocorticoid is dexamethasone sodium phosphate.

6. The use according to any one of claims 1-5, wherein the glucocorticoid is 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.

7. The use according to any one of claims 1-6, wherein:

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

b) the method comprises administering one or more further doses of a glucocorticoid.

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

9. The use according to claim 8, 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.

10. The use according to claim 8, 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.

11. The use according to claim 8, wherein the infectious disease is HIV or a disease resulting from infection with a coronavirus, such as COVID-19.

12. The use according to any one of claims 1-11, wherein the step of isolating is performed:

i) at least 48 hours after glucocorticoid administration; or

ii) between 48 hours and 13 days after glucocorticoid administration.

13. The use of claim 12, 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 method further comprises a step of expanding the isolated NKT-like cells;

c) the method further comprises a step of activating the isolated NKT-like cells;

d) the method further comprises a step of introducing a nucleic acid encoding a protein into the isolated NKT-like cells, and culturing the cells 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); and / or

e) the method further comprises a step of expanding the NKT-like cells.

14. Use of an isolated NKT-like cell for the manufacture of a medicament for use in a method of treating cancer, autoimmune disease, or infectious disease in a subject, the method comprising administering a therapeutically effective dose of an isolated NKT-like cell produced by a method as defined in any one of claims 1-13 to the subject;

wherein the isolated NKT-like cell is characterized in that it expresses: CD56, TCR gamma/delta, and iTCR; or, expresses TCR gamma/delta and iTCR.

15. An isolated NKT-like cell or population of NKT-like cells produced by a method as defined in any one of claims 1-14;

wherein the isolated NKT-like cell or population of NKT-like cells is 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.

16. 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

17. The isolated NKT-like cell or population of NKT-like cells according to claim 16, 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 .

18. The isolated NKT-like cell or population of NKT-like cells according to claim 16 or 17, 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.

19. Use of an isolated NKT-like cell according to any of claims 16-18 for the manufacture of a medicament for use in a method of treating cancer, autoimmune disease, or infectious disease in a subject, the method comprising administering a therapeutically effective dose of the isolated NKT-like cell to the subject.

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

wherein the glucocorticoid is dexamethasone or betamethasone; and

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 wherein:

the cancer is a myeloid leukemia or a solid tumor cancer selected from T cell lymphoma, squamous cell cancer, epithelial squamous cell cancer; small-cell lung cancer, adenocarcinoma of the lung and squamous carcinoma of the lung; cancer of the peritoneum; hepatocellular cancer; gastric or stomach cancer, including gastrointestinal cancer; glioblastoma; bladder cancer; hepatoma; colon cancer; rectal cancer; colorectal cancer; endometrial or uterine carcinoma; salivary gland carcinoma; vulval cancer; thyroid cancer; hepatic carcinoma; anal carcinoma; penile carcinoma; head and neck cancer; melanoma; pancreatic cancer; ovarian cancer; spleen cancer;

the autoimmune disease is systemic sclerosis; or

the infectious disease is a coronavirus, COVID-19, herpes, Varicella zoster virus, or human papilloma virus.