CLAIMS

1. A method of detecting a precursor of conventional dendritic cell (cDC) (pre-DC), comprising (i) determining the presence of a biomarker selected from a group consisting of:

(a) CD169 in combination with one or more biomarker(s) selected from a group consisting of~~, CD327,~~ AXL, CD271~~,~~ and CD324~~, and combinations thereof~~;

(b) CD327 in combination with one or more biomarker(s) selected from a group consisting of AXL, CD271 and CD324; and

(c) CD169 and CD327 in combination with one or more biomarker(s) selected from a group consisting of AXL, CD271 and CD324.

2. The method of claim 1, wherein the biomarker(s) is selected from a group consisting of:

~~(a) CD169;~~

~~(b) CD327;~~

~~(c) AXL;~~

~~(d) CD271;~~

~~(e) CD324;~~

~~(f) a combination of CD169, and CD327;~~

~~(g)~~(a) a combination of CD169, and AXL;

~~(h)~~(b) a combination of CD169, and CD271;

~~(i)~~(c) a combination of CD169, and CD324;

~~(j)~~(d) a combination of CD327, and AXL;

~~(k)~~(e) a combination of CD327, and CD271;

~~(l)~~(f) a combination of CD327, and CD324;

~~(m)a combination of AXL, and CD271;~~

~~(n) a combination of AXL, and CD324;~~

~~(o) a combination of CD271, and CD324;~~

~~(p)~~(g) a combination of CD169, CD327, and AXL;

~~(q)~~(h) a combination of CD169, CD327, and CD271;

~~(r)~~(i) a combination of CD169, CD327, and CD324;

~~(s)~~(j) a combination of CD169, AXL, and CD271;

~~(t)~~(k) a combination of CD169, AXL, and CD324;

~~(u)~~(l) a combination of CD169, CD271, and CD324;

~~(v)~~(m) a combination of CD327, AXL, and CD271;

~~(w)~~(n) a combination of CD327, AXL, and CD324;

~~(x)~~(o) a combination of CD327, CD271, and CD324;

~~(y) a combination of AXL, CD271, and CD324;~~

~~(z)~~(p) a combination of CD169, CD327, AXL, and CD271;

~~(aa)~~(q) a combination of CD169, CD327, AXL, and CD324;

~~(bb)~~(r) a combination of CD169, CD327, CD271, and CD324;

~~(cc)~~(s) a combination of CD169, AXL, CD271, and CD324;

~~(dd)~~(t) a combination of CD327, AXL, CD271, and CD324; and

~~(ee)~~(u) a combination of CD169, CD327, AXL, CD271, and CD324.

3. The method of claim 1 or 2, wherein step (i) comprises determining the presence of:

(A) CD169 and AXL to detect the early pre-DC cell population within the pre-DC cell population;

(B) CD169, CD271 and CD324, and wherein the method further comprises determining the presence of cell adhesion molecule 1 (CADM1) to detect pre-cDC1; or

(C) CD327, CD271 and CD324, and wherein the method further comprises determining the presence of a CD1c to detect pre-cDC2.

4. The method of claim 3, wherein (A) further ~~comprising~~comprises:

(ii) determining for the presence of one or more biomarkers selected from a group consisting of: HLA-DR, CD123, CD45RA, CD45, CD303, CD304, CD33, CD5, CX3CR1, CD2, and combinations thereof; and

(iii) determining for the absence of one or more biomarkers selected from a group consisting of: CD34, CD3, CD19/CD20, CD14, CD16, and combinations thereof,

prior to step (i) of claim 1.

~~5. The method of claim 1 or 2, wherein step (i) comprises determining the presence of CD169, and wherein the method further comprises determining the presence of cell adhesion molecule 1 (CADM1) to detect pre-cDC1.~~

~~6.~~5.The method of claim ~~5~~3, wherein (B) further comprises~~further comprising~~:

(ii) determining for the presence of one or more biomarkers selected from a group consisting of: HLA-DR, CD123, CD45RA, CD45, CD303, CD304, CD33, CX3CR1, CD2, CD5, and combinations thereof; and

(iii) determining for the absence of one or more biomarkers selected from a group consisting of: CD34, CD3, CD19/CD20, CD14, CD16, CD1c, and combinations thereof,

prior to step (i) of claim 3 part (B)~~5~~.

~~7. The method of claim 1 or 2, wherein step (i) comprises determining the presence of CD327, and wherein the method further comprises determining the presence of a CD1c to detect pre-cDC2.~~

~~8.~~6. The method of claim ~~7~~3, wherein (C) further comprises~~further comprising~~:

(ii) determining for the presence of one or more biomarkers selected from a group consisting of: HLA-DR, CD123, CD45RA, CD45, CD33, CX3CR1, CD2, CD5, and combinations thereof; and

(iii) determining for the absence of one or more biomarkers selected from a group consisting of: CD34, CD3, CD19/CD20, CD14, CD16, CADM1, and combinations thereof,

prior to step (i) of claim 3 part (C)~~7~~.

~~9.~~7. The method of any one of claims 1, 3 part (A), 3 part (B) or 3 part (C)~~5 or 7~~, further comprising determining the level of expression of any one or more of the biomarkers, wherein:

(I) (a) an increased expression level of any one or more biomarkers in any one of claims 1 or 4(ii) relative to a control indicates that the cell is an early pre-DC; and/or

(b) a decreased expression level of any one or more biomarkers in claim 4(iii) relative to a control indicates that the cell is an early pre-DC;

or

(II) (a) an increased expression level of any one or more biomarkers in any one of claims 1 or ~~6~~5(ii) relative to a control indicates that the cell is a pre-cDC1; and/or

(b) a decreased expression level of any one or more biomarkers in claim ~~6~~5(iii) relative to a control indicates that the cell is a pre-cDC1;

or

(III) (a) an increased expression level of any one or more biomarkers in any one of claims 1 or ~~8~~6(ii) relative to a control indicates that the cell is a pre-cDC2; and/or

(b) a decreased expression level of any one or more biomarkers in claim ~~8~~6(iii) relative to a control indicates that the cell is a pre-cDC2;

wherein the control comprises other cellular populations present or a pDC population that does not express CD169, CD327, AXL, CD271 and/or CD324.

~~10.~~8. The method of claim ~~9~~7, further comprising determining the change in the level of expression of any one or more of the biomarkers, wherein:

a) a change in the level of expression of any one or more of the biomarkers compared to the level of expression of any one or more of the biomarkers in a control indicates that the cell is an early pre-DC, pre-cDC1 or pre-cDC2; and

b) no change in the level of expression of any one or more of the biomarkers compared to the level of expression of any one or more of the biomarkers in a control indicates that the cell is not an early pre-DC, pre-cDC1 or pre-cDC2,

wherein the control comprises other cellular populations present or a pDC population that does not express CD169, CD327, AXL, CD271 and/or CD234.

~~11.~~9. The method of any one of claims 1 to ~~10~~8, wherein the detecting comprises contacting a sample suspected of containing pre-DC, comprising early pre-DC, pre-cDC1 and/or pre-cDC2 cells, with one or more binding molecule specific for the

biomarkers as defined in any one of claims 1 to ~~10~~8, selected from a group consisting of: an antibody, an antigen-binding fragment of an antibody, an aptamer and a ligand.

~~12.~~10. The method of claim ~~11~~9, wherein the binding molecule is coupled to a detectable label selected from a group consisting of: a fluorescent label, a radioactive label, a chemical label, an enzymatic label, a protein label, a magnetic label and a heavy metal.

~~13.~~11. The method of any one of claims 1 to ~~12~~10, wherein the detecting comprises mass cytometry or flow cytometry.

~~14.~~12. The method of any one of claims ~~11~~ 9 to ~~13~~11, wherein the sample is selected from a group consisting of: a blood sample; a tissue sample selected from a group consisting of bone marrow, lung, spleen, liver, heart, bone, skin, adipose tissue, dermis, intestine, urinary bladder, tendon, ligament, muscle, fascia, neurologic tissue, vessel, kidney, cartilage, sections of tissues such as biopsy and autopsy samples, frozen sections of tissues taken for histologic purposes, archival samples, explants and primary and/or transformed cell cultures derived from patient tissues and/or any other suitable tissue; a cell sample selected from a group consisting of peripheral blood mononuclear cells; and a bodily fluid sample selected from a group consisting of lymph fluids, cystic fluids, sputum, stool, tears, mucus, ascitic fluid, cystic fluid, urine, nipple exudates and nipple aspirates.

~~15.~~13. The method of any one of claims ~~11~~ 9 to ~~14~~12, wherein the sample is from a human subject.

~~16.~~14. The method of any one of claims 1 to ~~15~~13, further comprising the step of isolating the pre-DC cells detected using the method of any one of claims 1 to ~~15~~13.

~~17. A method of detecting a disease/condition, prognosis of an existing disease/condition, and/or determining the likelihood of an individual developing a disease/condition, comprising determining the number of pre-DC cells in a sample from a subject using the method of any one of claims 1 to 16, and comparing the determined number of cells to the number of pre-DC cells in a control sample, wherein a higher number of pre-DC cells in the sample from the subject compared to the number of pre-DC cells in the control sample indicates the presence of, or the likelihood of developing the disease/condition in the individual, wherein pre-DC comprises a cell selected from early pre-DC, pre-cDC1, pre-cDC2 and combinations thereof, and wherein the control sample is a sample selected from a group consisting of a sample obtained from the same patient prior to developing the disease/ condition, and a sample obtained from a healthy individual.~~

~~18. The method of claim 17, wherein the disease/condition is selected from a group consisting of: an inflammatory disease; obesity; cancer; an autoimmune disease ; an infectious disease and a metabolic disease/condition.~~

~~19. The method of claim 18, wherein the inflammatory disease is selected from a group consisting of lichen planus, atopic dermatitis and psoriasis; wherein the autoimmune disease is such as systemic lupus erythematosus; and wherein the infectious disease is selected from a group consisting of HIV, Zika, Chikungunya, hepatitis A, hepatitis B,~~

hepatitis C, viral hemorrhagic fevers, pox virus infections and mosquito borne encephalitis viruses.

20. A method of treating a patient determined to have a disease/condition according to the method of any one of claims 17 to 19, comprising administering to said patient an antibody selected from a group consisting of an anti-CD169 antibody or an antigen-binding fragment thereof, an anti-CD327 antibody or an antigen-binding fragment thereof, an anti-AXL antibody or an antigen binding fragment thereof, an anti-CD271 antibody or an antigen-binding fragment thereof, an anti-CD324 antibody or an antigen-binding fragment thereof, and combinations thereof.

21. The method of claim 20, wherein the disease is a disease whereby pathogenesis is caused by pre-DC, early pre-DC, pre-cDC1, pre-cDC2, or a combination thereof.

22. The method of claim 20 or 21, wherein the administration of said antibody or an antigen-binding fragment thereof causes depletion of a subset of cells selected from a group consisting of pre-DC, early pre-DC, pre-cDC1, pre-cDC2, or a combination thereof.

23. Use of an antibody or an antigen-binding fragment thereof in the manufacture of a medicament for treating a patient determined to have a disease/condition according to the method of any one of claims 17 to 19, wherein the antibody or an antigen-binding fragment thereof is selected from a group consisting of an anti-CD169 antibody or an antigen-binding fragment thereof, an anti-CD327 antibody or an antigen-binding fragment thereof, an anti-AXL antibody or an antigen-binding fragment thereof, an

anti-CD271 antibody or an antigen-binding fragment thereof, an anti-CD324 antibody or an antigen-binding fragment thereof, and combinations thereof.

24. An antibody or an antigen-binding fragment thereof, for use in treating a patient determined to have a disease/condition according to the method of any one of claims 17 to 19, wherein the antibody is selected from a group consisting of an anti-CD169 antibody or an antigen-binding fragment thereof, an anti-CD327 antibody or an antigen-binding fragment thereof, an anti-AXL antibody or an antigen-binding fragment thereof, an anti-CD271 antibody or an antigen-binding fragment thereof, an anti-CD324 antibody or an antigen-binding fragment thereof, and combinations thereof.

25. A kit for use in the method of any one of claims 1 to 19, wherein the kit comprises reagents for determining the presence of one or more biomarkers selected from the biomarkers listed in any one of claims 1 to 10, and wherein the kit further optionally comprises instructions for use.

26. An immunogenic composition comprising: (a) one or more binding molecules specific for one or more of the biomarkers as defined in any one of claims 1 to 19, or an antigen of a target disease and/or (b) one or more cells selected from the group consisting of early pre-DC, pre-cDC1, and pre-cDC2 detected using the methods of any one of claims 1 to 16.

27. The immunogenic composition of claim 26, wherein the one or more binding molecules are selected from a group consisting of an antibody, an antigen-binding fragment of an

~~antibody, scFV, aptamers, and a ligand derived from an infectious agent or cancer for generation of immune response for the purpose of vaccination against the disease.~~

~~28. The immunogenic composition of claim 26 or 27, further comprising an adjuvant, a preservative, a stabilizer, an encapsulating agent (e.g. lipid membranes, chitosan particles, biocompatible polymers) and/or a pharmaceutically acceptable carrier.~~

~~29. A method of eliciting an immune response against an infectious disease or cancer in a subject comprising administering the immunogenic composition of any one of claims 26 to 28.~~

~~30. The method of claim 29, wherein the infectious disease is selected from a group consisting of HIV, Zika, Chikungunya, hepatitis A, hepatitis B, hepatitis C, viral hemorrhagic fevers, pox virus infections and mosquito-borne encephalitis viruses.~~

~~31. The method of claim 29 or 30, wherein the immunogenic composition is to be administered by a route selected from a group consisting of intramuscular, intradermal, subcutaneous, intravenous, oral, and intranasal administration.~~

~~32. A method of detecting a precursor of conventional dendritic cell (cDC) (pre-DC) in a sample, wherein:~~

~~(I) the pre-DC comprises early pre-DC cells, and the method comprises the following steps in the following order:~~

~~(i) removing dead cells from the sample;~~

(ii) optionally isolating cells having a particular size, optionally 7-10 μm in diameter;

(iii) determining the presence of a CD45 biomarker and the absence of a CD34 biomarker;

(iv) determining the absence of CD3/19/20/14 and CD16 biomarkers;

(v) determining the presence of HLA-DR and CD123 biomarkers;

(vi) determining the presence of CD45RA and CD123 biomarkers; and

(vii) determining the presence of CD169, CD327, CD271 and/or CD324;

(II) the pre-DC comprises early pre-DC cells, and the method comprises the following steps in the following order:

(i) determining the presence of a CD45 biomarker and the absence of a CD34 biomarker;

(ii) determining the absence of CD3/19/20/14 and CD16 biomarkers;

(iii) determining the presence of HLA-DR and CD123 biomarkers;

(iv) determining the presence of CD45RA and CD33 biomarkers; and

(v) determining the presence of CD169, CD327, CD271 and/or CD324;

(III) the pre-DC comprises early pre-DC cells, and the method comprises the following steps in the following order:

(i) determining the presence of a CD45 biomarker and the absence of a CD34 biomarker;

(ii) determining the absence of CD3/19/20/14 and CD16 biomarkers;

(iii) determining the presence of HLA-DR and CD123 biomarkers;

(iv) determining the presence of CD45RA and CD33 biomarkers;

(v) determining the presence of CD45RA biomarker;

(vi) determining the absence of CADM1 biomarker; and

(vii) determining the presence of CD123 biomarker and the absence of CD1c biomarker;

(IV) the pre-DC comprises pre-cDC1 cells, and the method comprises the following steps in the following order:

(i) determining the presence of a CD45 biomarker and the absence of a CD34 biomarker;

(ii) determining the absence of CD3/19/20/14 and CD16 biomarkers;

(iii) determining the presence of HLA-DR and CD123 biomarkers;

(iv) determining the presence of CD45RA and CD33 biomarkers; and

(v) determining the presence of CADM1 and CD45RA biomarkers;

and

(V) the pre-DC comprises pre-cDC2 cells, and the method comprises the following steps in the following order:

(i) determining the presence of a CD45 biomarker and the absence of a CD34 biomarker;

(ii) determining the absence of CD3/19/20/14 and CD16 biomarkers;

(iii) determining the presence of HLA-DR and CD123 biomarkers;

(iv) determining the presence of CD45RA and CD33 biomarkers;

(v) determining the absence of CADM1 biomarker; and

(vi) determining the presence of CD1c and CD45RA biomarkers.