[0006] Human pDC and pre-DC express various common markers such as CD123, CD303, CD304 and CD45RA. These markers are commonly used to identify pDC. Therefore, these markers cannot be used to also identify pre-DC or distinguish pre-DC from pDC. Conventional gating strategies used for identification of pDC are not sufficient to discriminate human pre-DC from a cell population. Moreover, DC subsets, including pre-DC, have distinct functional specializations, hence some subsets could also serve as a potential biomarker to monitor progression of disease (e.g. changes in the number of cells in a certain subset could indicate a predisposition to specific inflammation and/or infection).

[0007] Therefore there is a need to provide means for detecting, identifying and isolating the early pre-DC, pre-cDC1 and/or pre-cDC2 subsets in human to overcome or at least ameliorate, one or more of the disadvantages described above.

[0008] There is a need to provide specific biomarkers or combinations of biomarkers for detecting, identifying and isolating the early pre-DC, pre-cDC1 and/or pre-cDC2 subsets in human which can clearly distinguish the subsets from other subsets of DC, or from each other, for further subset-specific studies or uses thereof.

[0009] There is also a need to provide means for modulating diseases or improving vaccination by targeting therapeutic compounds to the early pre-DC, pre-cDC1 and/or pre-cDC2 subsets to modulate, expand or deplete the subsets.

SUMMARY

[0010] According to a first example, there is provided a method of detecting a precursor of conventional dendritic cell (cDC) (pre-DC), comprising determining the presence of a

biomarker selected from a group consisting of CD169, CD327, AXL, CD271, CD324 and combinations thereof. In one aspect, the disclosure provides 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 AXL, CD271 and CD324; (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.

[0011] Advantageously, the method enables detection, identification and sorting of early pre-DC, pre-cDC1 and pre-cDC2, which were not possible prior to the present disclosure, allowing for a wide range of potential applications which are subset-specific. For example, it enables determination of the correlation between a specific subset (such as cell population size of a subset) with a specific disease.

[0012] According to a second example, there is provided 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 as disclosed herein, 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/ conditions, and a sample from a healthy individual.

[0013] According to a third example, there is provided a method of treating a patient determined to have a disease/condition according to the method as disclosed herein, 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.

[0014] Advantageously, the method allows for target-specific therapeutic applications.

[0015] According to a fourth example, there is provided a 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 as disclosed herein, 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.

[0016] According to a fifth example, there is provided an antibody or an antigen-binding fragment thereof for use in treating a patient determined to have a disease/condition according to the method as disclosed herein, 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.

[0017] According to a sixth example, there is provided a kit for use in the method as disclosed herein, wherein the kit comprises reagents for determining the presence of one or more biomarkers selected from the biomarkers as disclosed herein, and wherein the kit further optionally comprises instructions for use.

[0018] According to a seventh example, there is provided an immunogenic composition comprising: (a) one or more binding molecules specific for one or more of the biomarkers as

defined herein, (b) an antigen of a target disease and/or (c) one or more cells selected from the group consisting of pre-DC, pre-cDC1, and pre-cDC2.

[0019] According to an eighth example, there is provided a method of eliciting an immune response against an infectious disease or cancer in a subject comprising administering the immunogenic composition as disclosed herein.

[0020] According to a ninth example, there is provided 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: