METHOD OF IDENTIFYING PRO-INFLAMMATORY DENDRITIC CELLS

TECHNICAL FIELD

The present disclosure relates broadly to a method of characterising mononuclear phagocyte populations, such as dendritic cells, and related kits.

BACKGROUND

Mononuclear phagocytes (MNP) comprise a heterogeneous population of cells historically assigned to subsets based on their phenotype, ontogeny, transcriptomic profiles and their specialized functions. MNP comprise dendritic cell (DC) and monocyte subsets in the blood and tissues, as well as macrophages and monocyte-derived cells (MC) in tissues. It is important to clearly delineate these subsets to study their functions, as particular MNP subsets are increasingly recognized as having important roles in diseases. A clear method to identify these various subsets in the blood and tissues, as well as in health and disease, is challenging as their phenotypes are often overlapping.

DC and MC represent two complementary and integrated functional systems in time and space. DC specifically depend on FMS-like tyrosine kinase 3 (FLT3) for their differentiation and proliferation. They classically include plasmacytoid DC (pDC) that are highly specialized in type I interferon production, and conventional DC (cDC) that are major subsets involved in antigen presentation and modulation of immunity. Importantly, the DC nature of pDC is under debate, as they have been shown to differentiate from B-cell progenitors, and thus could be more related to the innate lymphoid cell family. cDC are further subdivided into two major lineages: cDC1, with superior antigen cross-presentation to $CD8^+$ T cells, and cDC2 that perform a wide spectrum of functions, including antigen presentation to $CD4^+$ T cells and priming to T helper 2 (Th2) and Th17-type responses. Importantly, DC subsets depend on critical transcription factors for their differentiation including IRF8 and BATF3 for cDC1

or IRF4 and KLF4 for cDC2. While cDC1 express several highly specific markers (CLEC9A, XCR1, CADM1) allowing their precise delineation, cDC2 express less specific defining markers that often overlap with monocytes.

Monocytes are highly heterogenous, plastic cells that patrol blood vessels and can migrate to tissues, where together with resident macrophages, they have central roles in tissue homeostasis maintenance and inflammation. Monocytes differentiate into MC with features characteristic of both macrophages and DC, the latter mostly during inflammation. MC can acquire a multitude of functional capabilities that are largely determined by the inflammatory milieu to which they are recruited. In human blood, monocyte subsets are defined based on their relative expression of CD14 and CD16 — two membrane proteins with supposed restricted expression to monocytes among all circulating MNP. Such restricted expression is now under debate, as in the blood, classical monocytes (cMo; $CD14^{hi}CD16^{-}$) and $CD1c^{+}$ cDC2 are phenotypically related and form a continuum, with cells falling in between that express markers of both cell types including the cDC2 marker CD1c, and the monocyte markers CD14 and CD11b. Similar intermediate pro-inflammatory cells also accumulate in inflamed tissues and while they seem to be derived from monocytes, they are functionally different due to their cDC2-specialized capacity to stimulate autologous $CD4^{+}$ T cells. Thus, understanding the currently debated nature of these cells could allow their manipulation in pathologic settings.

Thus, there is a need to provide an alternative method of characterising mononuclear phagocyte populations, such as dendritic cells, and related kits.

SUMMARY

In one aspect, there is provided a method of characterising dendritic cells, the method comprising: determining an expression of one or more of CD5, CD14 and CD163 in the dendritic cells.

In one embodiment, where the dendritic cells are determined to be $CD5^{-}$, $CD14^{+}$ and/or $CD163^{+}$, the method comprises identifying the dendritic cells as pro-inflammatory dendritic cells.

In one embodiment, wherein where the dendritic cells are determined to be $CD163^+CD14^+$, the method comprises identifying the dendritic cells as highly pro-inflammatory dendritic cells that are more pro-inflammatory than $CD163^-$ or $CD14^-$ dendritic cells.

In one embodiment, the method further comprises determining a proportion of $CD163^+CD14^+$ dendritic cells.

In one embodiment, the method further comprises determining an expression of one or more of CD11b, CD36, CD64, CD87, CD107a, CD206, CD274, CD354, $Fc\varepsilon RI\alpha$, HLA-DQ, CD2, CD59, CD81, CD166, CD229, CD271 and Integrin β7 in the dendritic cells.

In one embodiment, the dendritic cells have one or more of the following properties:

(i) is a conventional dendritic cell 2 (cDC2);

(ii) is dependent on IRF4 for differentiation;

(iii) is dependent on KLF4 for differentiation;

(iv) is dependent on FLT3 ligand (FLT3L) for differentiation; and

(v) is capable of activating and/or polarizing T cells.

In one aspect, there is provided a method of characterising inflammation and/or inflammatory disease in a subject, the method comprising: determining a proportion of $CD5^-$, $CD14^+$, $CD163^+$, and/or $CD14^+CD163^+$ dendritic cells in the subject's sample, wherein the proportion positively correlates with the level of inflammation and/or the severity of inflammatory disease in the subject.

In one embodiment, where the proportion of $CD5^-$, $CD14^+$, $CD163^+$, and/or $CD14^+CD163^+$ dendritic cells in the subject's sample is greater than a threshold proportion derived from a control sample, the method comprises identifying the presence of inflammation and/or inflammatory disease in the subject.

In one embodiment, where the proportion of $CD5^-$, $CD14^+$, $CD163^+$, and/or $CD14^+CD163^+$ dendritic cells in the sample is greater than the proportion in an earlier sample from the same subject, the method comprises identifying a worsening of inflammation and/or inflammatory disease in the subject, and wherein where the proportion of $CD5^-$, $CD14^+$, $CD163^+$, and/or $CD14^+CD163^+$ dendritic cells in the sample is lower than the proportion in the earlier sample, the

method comprises identifying an improvement of inflammation and/or inflammatory disease in the subject.

In one embodiment, the inflammatory disease is selected from the group consisting of systemic inflammatory disease, metabolic disorder, autoimmune disease and cancer.

In one embodiment, the inflammatory disease is selected from the group consisting of inflammatory skin disease, inflammatory bowel diseases, asthma, acute respiratory distress syndrome, chronic obstructive pulmonary disease, acute lung injury, bronchopulmonary dysplasia, cystic fibrosis, bronchitis, bronchiolitis, arthritis, osteoarthritis, ankylosing spondylitis and rheumatism.

In one embodiment, the metabolic disorder is selected from the group consisting of obesity, diabetes satiety and endocrine deficiencies related to aging.

In one embodiment, the autoimmune disease is selected from the group consisting of Systemic Lupus Erythematosus (SLE), diabetes, rheumatoid arthritis (RA), multiple sclerosis (MS), myasthenia gravis (MG), scleroderma, Crohn's disease, ulcerative colitis, Hashimoto's disease, Graves' disease, Sjögren's syndrome, polyendocrine failure, vitiligo, peripheral neuropathy, graft-versus-host disease, autoimmune polyglandular syndrome type I, acute glomerulonephritis, Addison's disease, adult-onset idiopathic hypoparathyroidism (AOIH), alopecia totalis, amyotrophic lateral sclerosis, ankylosing spondylitis, autoimmune aplastic anemia, autoimmune hemolytic anemia, Behcet's disease, Celiac disease, chronic active hepatitis, CREST syndrome, dermatomyositis, dilated cardiomyopathy, eosinophilia-myalgia syndrome, epidermolisis bullosa acquisita (EBA), giant cell arteritis, Goodpasture's syndrome, Guillain-Barré syndrome, hemochromatosis, Henoch-Schönlein purpura, idiopathic IgA nephropathy, insulin-dependent diabetes mellitus (IDDM), juvenile rheumatoid arthritis, Lambert-Eaton syndrome, linear IgA dermatosis, myocarditis, narcolepsy, necrotizing vasculitis, neonatal lupus syndrome (NLE), nephrotic syndrome, pemphigoid, pemphigus, polymyositis, primary sclerosing cholangitis, psoriasis, atopic dermatitis, rapidly-progressive glomerulonephritis (RPGN), Reiter's syndrome, stiff-man syndrome and thyroiditis.

In one embodiment, the autoimmune disease is selected from the group consisting of psoriasis, atopic dermatitis, Systemic Lupus Erythematosus (SLE) and systemic sclerosis (SSc).

In one embodiment, the cancer comprises a non-solid tumour, optionally wherein the non-solid tumor is selected from the group consisting of leukaemia, multiple myelomas and lymphomas.

In one embodiment, the cancer comprises a solid tumor, optionally wherein the solid tumour comprises sarcoma and/or carcinoma, further optionally wherein the sarcoma and/or carcinoma is selected from the group consisting of hepatocellular carcinoma, fibrosarcoma, myxosarcoma, liposarcoma, chondrosarcoma, osteogenic sarcoma, chordoma, angiosarcoma, endotheliosarcoma, lymphangiosarcoma, lymphangioendotheliosarcoma, synovioma, mesothelioma, Ewing's tumor, leiomyosarcoma, rhabdomyosarcoma, colon carcinoma, pancreatic cancer, breast cancer, ovarian cancer, prostate cancer, squamous cell carcinoma, basal cell carcinoma, adenocarcinoma, sweat gland carcinoma, sebaceous gland carcinoma, papillary carcinoma, papillary adenocarcinomas, cystadenocarcinoma, medullary carcinoma, bronchogenic carcinoma, renal cell carcinoma, hepatoma, bile duct carcinoma, choriocarcinoma, seminoma, embryonal carcinoma, Wilms' tumor, cervical cancer, testicular tumor, lung carcinoma, small cell lung carcinoma, bladder carcinoma, epithelial carcinoma, glioma, astrocytoma, medulloblastoma, craniopharyngioma, ependymoma, pinealoma, hemangioblastoma, acoustic neuroma, oligodendroglioma, meningioma, melanoma, neuroblastoma, and retinoblastoma.

In one embodiment, the cancer is selected from the group consisting of hepatocellular carcinoma, follicular lymphoma, small lymphocytic lymphoma, pancreatic tumour and breast cancer.

In one embodiment, wherein where the presence and/or the worsening of inflammation and/or an inflammatory disease in the subject is identified, the method further comprises allocating the subject to an inflammatory disease treatment regimen.

In one embodiment, the inflammatory disease treatment regimen comprises administering to the subject one or more agent selected from the group consisting of: an anti-inflammatory agent, an immunosuppressant agent, an anti-cancer agent, an inhibitor of FLT3L, an agent capable of binding to $CD5^-$, $CD14^+$, $CD163^+$, and/or $CD14^+CD163^+$ dendritic cells, an agent capable of neutralising $CD5^-$, $CD14^+$, $CD163^+$, and/or $CD14^+CD163^+$ dendritic cells, an antibody against $CD5^-$, $CD14^+$, $CD163^+$, and/or $CD14^+CD163^+$ dendritic cells, an agent capable of reducing the proportion of $CD5^-$, $CD14^+$, $CD163^+$, and/or $CD14^+CD163^+$ dendritic cells, an agent capable of reducing an activity of $CD5^-$, $CD14^+$, $CD163^+$, and/or $CD14^+CD163^+$ dendritic cells, an agent capable of reducing a number of a precursor of $CD5^-$, $CD14^+$, $CD163^+$, and/or $CD14^+CD163^+$ dendritic cells and an agent capable of inhibiting a differentiation of the precursor to $CD5^-$, $CD14^+$, $CD163^+$, and/or $CD14^+CD163^+$ dendritic cells.

In one aspect, there is provided a kit for characterising dendritic cells, inflammation and/or inflammatory disease, the kit comprising one or more reagent for detecting CD5, CD14 and/or CD163.

DEFINITIONS

The term “characterising” as used herein refers broadly to the identification of a nature and/or properties associated with a cell (e.g. a dendritic cell), a cell population, a tissue, a body response (e.g. an inflammation) or a disease (e.g. an inflammatory disease). The determination may be qualitative, quantitative or semi-quantitative

The term “treatment", "treat" and “therapy”, and synonyms thereof as used herein refer to both therapeutic treatment, prophylactic/preventative and/or palliative measures, wherein the object is to prevent or slow down (lessen) a medical condition, which includes but is not limited to diseases (such as inflammatory diseases), symptoms and disorders. A medical condition also includes a body’s response to a disease or disorder, e.g. inflammation. Those in need of such treatment include those already with a medical condition as well as

those prone to getting the medical condition or those in whom a medical condition is to be prevented.

The term “subject” as used herein includes patients and non-patients. The term “patient” refers to individuals suffering or are likely to suffer from a medical condition such as inflammation or inflammatory disease, while “non-patients” refer to individuals not suffering and are likely to not suffer from the medical condition. “Non-patients” include healthy individuals, non-diseased individuals and/or an individual free from the medical condition. The term “subject” includes humans and animals. Animals include murine and the like. “Murine” refers to any mammal from the family Muridae, such as mouse, rat, and the like.

The term "micro" as used herein is to be interpreted broadly to include dimensions from about 1 micron to about 1000 microns.

The term "nano" as used herein is to be interpreted broadly to include dimensions less than about 1000 nm.

The term “particle” as used herein broadly refers to a discrete entity or a discrete body. The particle described herein can include an organic, an inorganic or a biological particle. The particle used described herein may also be a macro-particle that is formed by an aggregate of a plurality of sub-particles or a fragment of a small object. The particle of the present disclosure may be spherical, substantially spherical, or non-spherical, such as irregularly shaped particles or ellipsoidally shaped particles. The term “size” when used to refer to the particle broadly refers to the largest dimension of the particle. For example, when the particle is substantially spherical, the term “size” can refer to the diameter of the particle; or when the particle is substantially non-spherical, the term “size” can refer to the largest length of the particle.

The terms "coupled" or "connected" as used in this description are intended to cover both directly connected or connected through one or more intermediate means, unless otherwise stated.

The term "associated with", used herein when referring to two elements refers to a broad relationship between the two elements. The relationship includes, but is not limited to a physical, a chemical or a biological relationship. For example, when element A is associated with element B, elements A and B

may be directly or indirectly attached to each other or element A may contain element B or vice versa.

The term "adjacent" used herein when referring to two elements refers to one element being in close proximity to another element and may be but is not limited to the elements contacting each other or may further include the elements being separated by one or more further elements disposed therebetween.

The term "and/or", e.g., "X and/or Y" is understood to mean either "X and Y" or "X or Y" and should be taken to provide explicit support for both meanings or for either meaning.

Further, in the description herein, the word “substantially” whenever used is understood to include, but not restricted to, "entirely" or “completely” and the like. In addition, terms such as "comprising", "comprise", and the like whenever used, are intended to be non-restricting descriptive language in that they broadly include elements/components recited after such terms, in addition to other components not explicitly recited. For example, when “comprising” is used, reference to a “one” feature is also intended to be a reference to “at least one” of that feature. Terms such as “consisting”, “consist”, and the like, may in the appropriate context, be considered as a subset of terms such as "comprising", "comprise", and the like. Therefore, in embodiments disclosed herein using the terms such as "comprising", "comprise", and the like, it will be appreciated that these embodiments provide teaching for corresponding embodiments using terms such as “consisting”, “consist”, and the like. Further, terms such as "about", "approximately" and the like whenever used, typically means a reasonable variation, for example a variation of +/- 5% of the disclosed value, or a variance of 4% of the disclosed value, or a variance of 3% of the disclosed value, a variance of 2% of the disclosed value or a variance of 1% of the disclosed value.

Furthermore, in the description herein, certain values may be disclosed in a range. The values showing the end points of a range are intended to illustrate a preferred range. Whenever a range has been described, it is intended that the range covers and teaches all possible sub-ranges as well as individual numerical values within that range. That is, the end points of a range should not be interpreted as inflexible limitations. For example, a description of a range of 1%

to 5% is intended to have specifically disclosed sub-ranges 1% to 2%, 1% to 3%, 1% to 4%, 2% to 3% etc., as well as individually, values within that range such as 1%, 2%, 3%, 4% and 5%. The intention of the above specific disclosure is applicable to any depth/breadth of a range.

Additionally, when describing some embodiments, the disclosure may have disclosed a method and/or process as a particular sequence of steps. However, unless otherwise required, it will be appreciated that the method or process should not be limited to the particular sequence of steps disclosed. Other sequences of steps may be possible. The particular order of the steps disclosed herein should not be construed as undue limitations. Unless otherwise required, a method and/or process disclosed herein should not be limited to the steps being carried out in the order written. The sequence of steps may be varied and still remain within the scope of the disclosure.

Furthermore, it will be appreciated that while the present disclosure provides embodiments having one or more of the features/characteristics discussed herein, one or more of these features/characteristics may also be disclaimed in other alternative embodiments and the present disclosure provides support for such disclaimers and these associated alternative embodiments.

DESCRIPTION OF EMBODIMENTS

Exemplary, non-limiting embodiments of a method of characterising mononuclear phagocyte populations, such as dendritic cells, and related kits are disclosed hereinafter.

In various embodiments, there is provided a method of characterising mononuclear phagocyte (MNP) populations. Examples of mononuclear phagocyte populations include dendritic cells (DC), monocytes, macrophages and monocyte-derived cells (MC). Characterising MNP population(s) may comprise identifying a nature and/or a property associated with the MNP population(s). In various embodiments, characterising the MNP populations comprises subsetting the populations based on one or more of their phenotypes, ontogenies, transcriptomic profiles and specialized functions. In various

embodiments, characterising the MNP populations comprises determining a type (including a subtype), an expression profile, and/or a property (e.g. an ability/capability and/or propensity to induce/promote inflammation) associated with the MNP populations. In some embodiments, characterising MNP population(s) comprises determining a type or a subtype of the MNP population(s). For example, characterising MNP populations may comprise distinguishing dendritic cells from monocytes. For example, characterising a dendritic cell, optionally a cDC2 dendritic cell, may comprise identifying a subtype of the dendritic cell, optionally the cDC2 dendritic cell. In some embodiments, an MNP population is characterised by its ability and/or propensity to induce inflammation. In some embodiments, an MNP population is characterised by its expression of one or more biomarkers.

In various embodiments, the method comprises determining and/or detecting and/or quantifying an expression and/or a level of at least about one, at least about two, at least about three, at least about four, at least about five, at least about six, at least about seven, at least about eight, at least about nine or at least about ten nucleic acids/genes/proteins/markers in the MNP population(s). In various embodiments, the method comprises determining an expression of no more than about ten, no more than about nine, no more than about eight, no more than about seven, no more than about six, no more than about five, no more than about four, no more than about three, no more than about two or no more than about one nucleic acid/ gene/protein/marker in the MNP population(s).

In various embodiments, the nucleic acid/gene/protein/marker is selected from the group consisting of AXL, BLTA, BTLA, CD101, CD107a, CD109, CD112, CD115, CD11b, CD124, CD14, CD155, CD163, CD166, CD172a, CD180, CD183, CD195, CD1c, CD1d, CD2, CD200, CD200R, CD206, CD218a, CD22, CD229, CD26, CD271, CD274, CD282, CD303, CD324, CD34, CD354, CD36, CD45RA, CD5, CD56, CD59, CD63, CD64, CD71, CD74, CD81, CD84, CD87, CD87 , CD88, CD89, CD95, CLEC12A, CLEC4E, DNAI2, FcεRIα , HLA-DQ, Igk, Integrin β7, LTB (Lymphotoxin-b), MEX3B, NOTCH2, NUMBL, RN7SL846P, S100A13, S100A8, S100A9, S100A9, SIGLEC6 (CD327) and combinations thereof.

In various embodiments, the nucleic acid/gene/protein/marker comprises a surface nucleic acid/gene/protein/marker. In various embodiments, the nucleic acid/gene/protein/marker comprises a membrane nucleic acid/gene/protein/marker.

In one embodiment, the MNP population comprises dendritic cells. The dendritic cells may be a population that circulate in the blood tissue.

In various embodiments therefore, there is provided a method of characterising dendritic cells. A method of characterising dendritic cells may include a method of identifying/determining a presence or absence of dendritic cells, a method of identifying/determining a subtype of dendritic cells, a method of classifying dendritic cells, a method of identifying/determining a property of dendritic cells, a method of identifying/determining a function of dendritic cells, a method of identifying/determining an expression profile, an expression signature and/or a transcriptomic profile of dendritic cells, a method of identifying/determining a phenotype of dendritic cells, a method of identifying/determining an ontogeny of dendritic cells and the like. In some embodiments, a method of identifying/determining a property of dendritic cells includes identifying/determining an ability of the dendritic cells to induce inflammation or a pro-inflammatory effect of the dendritic cells. In various embodiments, the identification/determination can be qualitative, quantitative or semi-quantitative.

In various embodiments, the method comprises determining and/or detecting and/or quantifying an expression and/or a level of one or more of CD5, CD14 and CD163 in the dendritic cells.

In various embodiments therefore, there is provided a method of characterising dendritic cells, the method comprising determining an expression of one or more of CD5, CD14 and CD163 in the dendritic cells. In some embodiments, the method comprises determining an expression of two or more of CD5, CD14 and CD163 in the dendritic cells. In some embodiments, the method comprises determining an expression of CD5, CD14 and CD163 in the dendritic cells.

In some embodiments, the method comprises determining an expression of CD5 and one or more of CD14 and CD163. In some embodiments, the method comprises determining an expression of CD14 and one or more of CD5 and CD163. In some embodiments, the method comprises determining an expression of CD163 and one or more of CD5 and CD14.

In various examples, $CD5^{-/lo}$ dendritic cells are more pro-inflammatory than $CD5^{+/hi}$ dendritic cells. In various examples, $CD14^{+/hi}$ dendritic cells are more pro-inflammatory than $CD14^{-/lo}$ dendritic cells. In various examples, $CD163^{+/hi}$ dendritic cells are more pro-inflammatory than $CD163^{-/lo}$ dendritic cells. In various examples, $CD163^{+/hi}CD14^{+/hi}$ dendritic cells are more pro-inflammatory than $CD163^{-/lo}$, $CD14^{-/lo}$, $CD163^{+/hi}CD14^{-/lo}$ and/or $CD163^{-/lo}CD14^{-/lo}$ dendritic cells. In various examples, $CD5^{-/lo}CD163^{+/hi}CD14^{+/hi}$ dendritic cells more pro-inflammatory than $CD5^{+/hi}$, $CD5^{+/hi}CD163^{-/lo}CD14^{-/lo}$, $CD163^{-/lo}$, $CD14^{-/lo}$, $CD163^{+/hi}CD14^{-/lo}$, $CD163^{-/lo}CD14^{-/lo}$, $CD5^{-/lo}CD163^{-/lo}$, $CD5^{-/lo}$ $CD14^{-/lo}$, $CD5^{-/lo}CD163^{+/hi}CD14^{-/lo}$ and $CD5^{-/lo}CD163^{-/lo}CD14^{-/lo}$ dendritic cells. In various examples, $CD5^{-/lo}CD163^{+/hi}CD14^{-/lo}$ dendritic cells are more pro-inflammatory than $CD5^{-/lo}CD163^{-/lo}$ and $CD5^{-/lo}CD163^{-/lo}CD14^{-/lo}$ dendritic cells. Advantageously, the method may allow for the identification of dendritic cells having different capabilities or tendencies or propensities to induce/promote inflammation.

In various embodiments, an absence of CD5 expression or a substantially low CD5 expression, a presence of CD14 expression or a substantially high CD14 expression and/or a presence of CD163 expression or a substantially high CD163 expression in the dendritic cells is indicative that the dendritic cells are capable of inducing inflammation or that the dendritic cells are pro-inflammatory. In various embodiments therefore, wherein where the dendritic cells are determined to be $CD5^-$, $CD14^+$ and/or $CD163^+$, the method further comprises identifying the dendritic cells as pro-inflammatory dendritic cells. In various embodiments, wherein where the dendritic cells are determined to be $CD163^+CD14^+$, the method comprises identifying the dendritic cells as highly pro-inflammatory dendritic cells. In various embodiments, highly pro-inflammatory dendritic cells are more pro-inflammatory than $CD163^-$ or $CD14^-$ dendritic cells. In various embodiments, wherein where the dendritic cells are determined to be $CD5^-$

$CD163^{+}CD14^{+}$, the method comprises identifying the dendritic cells as highly pro-inflammatory dendritic cells.

In various embodiments, the method further comprises determining a level and/or a proportion of dendritic cells expressing $CD5^{-/lo}CD163^{+/hi}CD14^{+/hi}$, $CD5^{+/hi}$, $CD5^{+/hi}CD163^{-/lo}CD14^{-/lo}$, $CD163^{-/lo}$, $CD14^{-/lo}$, $CD163^{-/lo}CD14^{+/hi}$, $CD163^{+/hi}CD14^{-/lo}$, $CD163^{-/lo}CD14^{-/lo}$, $CD5^{-/lo}CD163^{-/lo}$, $CD5^{-/lo}CD14^{-/lo}$, $CD5^{-/lo}CD163^{-/lo}CD14^{+/hi}$, $CD5^{-/lo}CD163^{+/hi}CD14^{-/lo}$ and/or $CD5^{-/lo}CD163^{-/lo}CD14^{-/lo}$. In some embodiments, the method comprises determining a level and/or a proportion of $CD5^{+}$, $CD5^{-}CD163^{-}$, $CD5^{-}CD163^{+}CD14^{-}$ and/or $CD5^{-}CD163^{+}CD14^{+}$ dendritic cells. In one embodiment, the method comprises determining a proportion of $CD163^{+}CD14^{+}$ dendritic cells. In one embodiment, the method comprises determining a proportion of $CD5^{-}CD163^{+}CD14^{+}$ dendritic cells. As used herein, the term "proportion" refers to the ratio of the specified dendritic cells to the total number of dendritic cells in a population or subpopulation. In some embodiments, a proportion of $CD5^{-}CD163^{+}CD14^{+}$ dendritic cells refers to the ratio of the $CD5^{-}CD163^{+}CD14^{+}$ dendritic cells to the total number of conventional dendritic cell 2 (cDC2). In some embodiments, a proportion of $CD5^{-}CD163^{+}CD14^{+}$ dendritic cells refers to the ratio of the $CD5^{-}CD163^{+}CD14^{+}$ dendritic cells to the total number of a subpopulation of dendritic cells having one or more of the following properties: (i) is a conventional dendritic cell 2 (cDC2); (ii) is dependent on IRF4 for differentiation; (iii) is dependent on KLF4 for differentiation; (iv) is dependent on FLT3 ligand (FLT3L) for differentiation; and (v) is capable of activating and/or polarizing T cells e.g. naïve T cells or allogeneic naïve $CD4^{+}$ T cells.

In some examples, the dendritic cells, e.g. dendritic cells expressing CD163, express one or more nucleic acids/genes/proteins/markers selected from the group consisting of CD5, CD14, CD11b, CD36, CD64, CD87, CD107a, CD206, CD274, CD354, FcεRIα, HLA-DQ, CD2, CD59, CD81, CD166, CD229, CD271, and Integrin β7. In some examples, the dendritic cells, e.g. dendritic cells expressing CD163, express one or more nucleic acids/genes/proteins/markers selected from the group consisting of FcεRIα, HLA-DQ, CD2, CD59, CD81, CD166, CD229, CD271, and Integrin β7. In some examples, the dendritic cells,

e.g. dendritic cells expressing CD163, express one or more nucleic acids/genes/proteins/markers selected from the group consisting of CD56, CD5, CD303, CD271, CD22, CD124, CD324, integrin β7, BTLA, CD26, CD183, CD71, CD59, CD218a, CD200, CD195, CD1c, CD282, CD107a, CD11b, CD274, CD14, CD166, CD81, CLEC12A, CD63, CD84, CD115, CD95, CD163, CD112, CD155, CD206, CD172a, CD354, CD36, CD64, and CD87. In some examples, the dendritic cells, e.g. dendritic cells expressing CD163, may highly express DNAI2, MEX3B, RN7SL846P, NUMBL, CD109, S100A8, S100A9, CD14, CLEC4E, and/or S100A13.

In some examples, the dendritic cells, e.g. $CD5^+$ $CD163^+$ $CD14^+$ dendritic cells, has the following phenotype (one or more nucleic acids/genes/proteins/markers selected) from the group consisting of $CD56^-$, $CD5^-$, $CD303^-$, $CD271^-$, $CD22^-$, $CD124^-$, $CD324^-$, integrin $\beta7^-$, $BTLA^-$, $CD26^-$, $CD183^-$, $CD71^-$, $CD59^-$, $CD218a^-$, $CD200^-$, $CD195^-$, $CD1c^-$, $CD282^{int}$, $CD107a^{int}$, $CD11b^{int}$, $CD274^+$, $CD14^+$, $CD166^-$, $CD81^-$, $CLEC12A^+$, $CD63^+$, $CD84^+$, $CD115^+$, $CD95^+$, $CD163^+$, $CD34^-$, $CD112^+$, $CD155^+$, $CD206^+$, $CD172a^+$, $CD354^+$, $CD36^+$, Igk^+, $CD64^+$, and $CD87^+$. In some examples, the dendritic cells, e.g. $CD163^+$ $CD14^+$ dendritic cells, expresses one or more nucleic acids/genes/proteins/markers selected from the group consisting of $CD56^-$, $CD5^-$, $CD303^-$, $CD271^-$, $CD22^-$, $CD124^-$, $CD324^-$, integrin $\beta7^-$, $BTLA^-$, $CD26^-$, $CD183^-$, $CD71^-$, $CD59^-$, $CD218a^-$, $CD200^-$, $CD195^-$, $CD1c^-$, $CD282^{int}$, $CD107a^{int}$, $CD11b^{int}$, $CD274^+$, $CD14^+$, $CD166^-$, $CD81^-$, $CLEC12A^+$, $CD63^+$, $CD84^+$, $CD115^+$, $CD95^+$, $CD163^+$, $CD34^-$, $CD112^+$, $CD155^+$, $CD206^+$, $CD172a^+$, $CD354^+$, $CD36^+$, Igk^+, $CD64^+$, and $CD87^+$.

In some examples, the dendritic cells, e.g $CD163^+$ $CD14^-$ dendritic cells, has the following phenotype (one or more nucleic acids/genes/proteins/markers selected) from the group consisting of $CD56^-$, $CD5^-$, $CD303^-$, $CD271^-$, $CD22^-$, $CD124^-$, $CD324^-$, integrin $\beta7^-$, $BTLA^-$, $CD26^-$, $CD183^-$, $CD71^{int}$, $CD59^+$, $CD218a^-$, $CD200^-$, $CD195^-$, $CD1c^-$, $CD282^-$, $CD107a^-$, $CD11b^-$, $CD274^-$, $CD14^-$, $CD166^+$, $CD81^+$, $CLEC12A^+$, $CD63^+$, $CD84^+$, $CD115^+$, $CD95^+$, $CD163^+$, $CD112^+$, $CD155^+$, $CD206^+$, $CD172a^+$, $CD354^+$, $CD36^{int}$, $CD64^-$, and $CD87^-$. In some examples, the dendritic cells, e.g $CD163^+$ $CD14^-$ dendritic cells, express one or more nucleic acids/genes/proteins/markers selected from the group consisting of $CD56^-$, $CD5^-$

, $CD303^-$, $CD271^-$, $CD22^-$, $CD124^-$, $CD324^-$, integrin $\beta7^-$, $BTLA^-$, $CD26^-$, $CD183^-$, $CD71^{int}$, $CD59^+$, $CD218a^-$, $CD200^-$, $CD195^-$, $CD1c^-$, $CD282^-$, $CD107a^-$, $CD11b^-$, $CD274^-$, $CD14^-$, $CD166^+$, $CD81^+$, $CLEC12A^+$, $CD63^+$, $CD84^+$, $CD115^+$, $CD95^+$, $CD163^+$, $CD112^+$, $CD155^+$, $CD206^+$, $CD172a^+$, $CD354^+$, $CD36^{int}$, $CD64^-$, and $CD87^-$.

In some examples, the dendritic cells, e.g the $CD5^-CD163^+CD14^+$ dendritic cells, express one or more nucleic acids/genes/proteins/markers selected from the group consisting of nucleic acids/genes/proteins/markers involved in dendritic cell maturation, production of nitric and reactive oxygen species (NOS and ROS) in macrophages, phagosome formation, death receptor signalling, inflammasome pathway, autophagy pathways, as well as systemic lupus erythematosus (SLE) signalling. In some examples, the dendritic cell as described herein expresses the nucleic acids/genes/proteins as illustrated in FIG. 10 (such as FIG. 10D, 10G).

In various embodiments therefore, the method further comprises determining an expression of one or more of the above listed nucleic acids/genes/proteins/markers in the dendritic cells. In some embodiments, the method comprises determining an expression of one or more of AXL, BLTA, CD1c, CD1d, CD5, CD11b, CD64, CD74, CD88, CD89, CD101, CD109, CD180, CD200R, CD45RA, FcεRIα FcεRIα, HLA-DQ, Integrin β7, LTB (Lymphotoxin-β), NOTCH2, S100A8, S100A9 and SIGLEC6 (CD327) in the dendritic cells. In some embodiments, the method further comprises determining an expression of one or more of CD11b, CD36, CD64, CD87, CD107a, CD206, CD274, CD354, FcεRIα, HLA-DQ, CD2, CD59, CD81, CD166, CD229, CD271 and Integrin β7 in the dendritic cells.

In some examples, the $CD5^-CD163^+CD14^+$ cell is one of the largest cells, is rough and has more granular membrane as compared to $CD5^+$, $CD163^-$ and/or $CD14^-$ dendritic cells, and other MNP populations such as monocytes (as can be observed in the forward scatter (FSC-A) and side scatter (SSC-A) view in a flow cytometry analysis). In various embodiments therefore, the method further comprises determining an appearance or morphology of the dendritic cells including but not limited to the size, roughness and granularity.

In various embodiments, the dendritic cells comprise cDC2 cells. In various embodiments, the dendritic cells have one or more of the following properties: (i) is a conventional dendritic cell 2 (cDC2); (ii) is dependent on IRF4 for differentiation; (iii) is dependent on KLF4 for differentiation; (iv) is dependent on FLT3 ligand (FLT3L) for differentiation; and (v) is capable of activating and/or polarizing T cells e.g. naïve T cells or allogeneic naïve $CD4^+$ T cells.

In various embodiments, the determining and/or detecting and/or quantifying is via a marker cell sorting such as magnetic beads cell sorting, fluorescence-activated cell sorting, flow cytometry, ELISA, Western Blotting, immunohistochemistry, and the like. In some examples, the determining and/or detecting and/or quantifying is via flow cytometry. In various embodiments, the determining and/or detecting and/or quantifying is performed to detect protein expression and/or intracellular gene transcription expression. In various embodiments, the determining and/or detecting and/or quantifying is via methods for detecting amplification products, such as, but is not limited to, PCR, RT-PCR, q-PCR, and the like. It will be appreciated that other suitable methods of detecting a nucleic acid/gene/protein/marker that are known in the art may also be used.

In various embodiments, there is provided a method of distinguishing pro-inflammatory dendritic cells from the less or non- pro-inflammatory dendritic cells, the method comprising determining an expression of one or more CD5, CD14 and/or CD163 in the dendritic cells. In various embodiments, an absence of CD5 expression or a substantially low CD5 expression, a presence of CD14 expression or a substantially high CD14 expression and/or a presence of CD163 expression or a substantially high CD163 expression in the dendritic cells is indicative that the dendritic cells are pro-inflammatory. In various embodiments, there is provided a method of distinguishing a pro-inflammatory subpopulation of dendritic cells (e.g. $CD163^+$ DC3) from the less or non- pro-inflammatory subpopulation of dendritic cells (e.g. $CD5^+$ DC2), the method comprising determining an expression of one or more of CD14, CD11b, CD36, CD64, CD87, CD107a, CD206, CD274 and CD354 in the dendritic cells, wherein an expression and/or substantially high expression of one or more of the markers is indicative

that the cells are pro-inflammatory dendritic cells, optionally $CD163^+$ dendritic cells, optionally $CD163^+$ DC3 cells.

In various embodiments, there is provided a method of distinguishing dendritic cells from other MNP populations such as monocytes, macrophages and monocyte-derived cells. In one embodiment, the method comprises determining an expression of one or more CD5, CD14 and/or CD163 in the cells. In one embodiment, the method comprises distinguishing dendritic cells from monocytes, the method comprising determining an expression of one or more of HLA-DQ, FcεRIα, CD88 and CD89 in the cells. In various embodiments, an absence of CD88 expression or a substantially low CD88 expression, an absence of CD89 expression or a substantially low CD89 expression, a presence of HLA-DQ expression or a substantially high HLA-DQ expression and/or a presence of FcεRIα expression or a substantially high FcεRIα expression is indicative that the cells are dendritic cells. In various embodiments, an absence of HLA-DQ expression or a substantially low HLA-DQ expression, an absence of FcεRIα expression or a substantially low FcεRIα expression, a presence of CD88 expression or a substantially high CD88 expression and/or a presence of CD89 expression or a substantially high CD89 expression is indicative that the cells are monocytes. In various embodiments, the method comprises determining an expression of one or more of FcεRIα, HLA-DQ, CD2, CD59, CD81, CD166, CD229, CD271 and Integrin β7 in the cells, wherein an expression and/or substantially high expression of one or more of the markers is indicative that the cells are dendritic cells, optionally inflammatory dendritic cells, optionally DC3 cells. In various embodiments, the method comprises determining an expression of one or more markers selected from the group consisting of FcεRIα, HLA-DQ, CD2, CD59, CD81, CD166, CD229, CD271 and Integrin β7, and one or more markers selected from the group consisting of CD14, CD11b, CD36, CD64, CD87, CD107a, CD206, CD274 and CD354.

In various embodiments, there is provided a method of separating/isolating/extracting pro-inflammatory dendritic cells e.g. from less or non- pro-inflammatory dendritic cells, the method comprising contacting the dendritic cells with an agent, e.g. a capture agent, capable of recognising and/or

binding to one or more of CD5, CD14 and/or CD163. In some embodiments, the method further comprises contacting the dendritic cells with an agent, e.g. a capture agent, capable of recognising and/or binding to one or more nucleic acid/gene/protein/marker selected from the group consisting of AXL, BLTA, BTLA, CD101, CD107a, CD109, CD112, CD115, CD11b, CD124, CD14, CD155, CD163, CD166, CD172a, CD180, CD183, CD195, CD1c, CD1d, CD2, CD200, CD200R, CD206, CD218a, CD22, CD229, CD26, CD271, CD274, CD282, CD303, CD324, CD34, CD354, CD36, CD45RA, CD5, CD56, CD59, CD63, CD64, CD71, CD74, CD81, CD84, CD87, CD87 , CD88, CD89, CD95, CLEC12A, CLEC4E, DNAI2, FcεRIα , HLA-DQ, Igk, Integrin β7, LTB (Lymphotoxin-b), MEX3B, NOTCH2, NUMBL, RN7SL846P, S100A13, S100A8, S100A9, S100A9, SIGLEC6 (CD327) and combinations thereof.

In various embodiments, the method of characterising dendritic cells may also be useful for characterising a body response such as inflammation and/or a disease such as an inflammatory disease in a subject since certain dendritic cells may be associated with the body response and/or the disease. Thus, when characterising a body response such as inflammation and/or or a disease such as an inflammatory disease in a subject, the subject's sample may be collected, and the dendritic cells contained in the sample may be characterised to identify (e.g. qualitatively, quantitatively or semi- quantitatively) any dendritic cells that may be pro-inflammatory or associated with the body response and/or the disease. In various embodiments, characterising the dendritic cells in a subject's sample, e.g. identifying/measuring a presence/amount/level/proportion of pro-inflammatory dendritic cells in the sample, may give an indication of the presence or absence of a body response such as inflammation and/or or a disease such as an inflammatory disease in the subject. In various embodiments, characterising the dendritic cells in a subject's sample, e.g. identifying/measuring a presence/amount /level/proportion in a subject's sample may give an indication of a level/severity/extent/burden/aggressiveness/disease stage/disease state a body response such as inflammation and/or or a disease such as an inflammatory disease in the subject.

In various embodiments, characterising a body response in the form of an inflammation and/or a disease such as an inflammatory disease in a subject may include determining a presence or an absence of the body response and/or the disease in the subject, determining the subject's susceptibility to the body response and/or the disease, determining a level/severity/extent/burden/aggressiveness/disease stage/disease state of the body response and/or the disease in the subject, diagnosing the body response and/or the disease in the subject, determining a prognosis of the body response and/or the disease in the subject, and determining an improvement and/or a worsening of the body response and/or the disease in the subject.

Thus, in various embodiments, there is provided a method of characterising inflammation and/or inflammatory disease in a subject, the method comprising determining an expression of one or more of CD5, CD14 and CD163. In various embodiments, there is provided a method of characterising inflammation and/or inflammatory disease in a subject, the method comprising determining a level or a proportion of dendritic cells expressing $CD5^{-/lo}CD163^{+/hi}CD14^{+/hi}$, $CD5^{+/hi}$, $CD5^{+/hi}CD163^{-/lo}CD14^{-/lo}$, $CD163^{-/lo}$, $CD14^{-/lo}$, $CD163^{-/lo}CD14^{+/hi}$, $CD163^{+/hi}CD14^{-/lo}$, $CD163^{-/lo}CD14^{-/lo}$, $CD5^{-/lo}CD163^{-/lo}$, $CD5^{-/lo}$ $CD14^{-/lo}$, $CD5^{-/lo}CD163^{-/lo}CD14^{+/hi}$, $CD5^{-/lo}CD163^{+/hi}CD14^{-/lo}$ and/or $CD5^{-/lo}CD163^{-/lo}CD14^{-/lo}$. In some embodiments, the method comprises determining a level or a proportion of $CD5^{-}$, $CD14^{+}$, $CD163^{+}$, and/or $CD14^{+}CD163^{+}$ dendritic cells. In some embodiments, the method comprises determining a level or a proportion of $CD5^{-}$, $CD14^{+}$, $CD163^{+}$, $CD14^{+}CD163^{+}$, $CD5^{-}CD163^{-}$, $CD5^{-}CD163^{+}CD14^{-}$ and/or $CD5^{-}CD163^{+}CD14^{+}$ dendritic cells. In one embodiment, the method comprises determining a proportion of $CD163^{+}CD14^{+}$ dendritic cells. In one embodiment, the method comprises determining a proportion of $CD5^{-}CD163^{+}CD14^{+}$ dendritic cells. In some examples, the level or proportion of the dendritic cells correlates, e.g. positively correlates, with the level of inflammation and/or the severity of inflammatory disease in the subject.

In various embodiments, there is provided a method of characterising inflammation and/or inflammatory disease in a subject, the method comprising:

determining a proportion of $CD5^-$, $CD14^+$, $CD163^+$, $CD14^+CD163^+$ and/or $CD5^-CD14^+CD163^+$ dendritic cells in the subject's sample, wherein the proportion positively correlates with the level of inflammation and/or the severity of inflammatory disease in the subject.

In various embodiments, wherein where the proportion of $CD5^-$, $CD14^+$, $CD163^+$, $CD14^+CD163^+$ and/or $CD5^-CD14^+CD163^+$ dendritic cells in the subject's sample is greater than a threshold proportion derived from a control sample, the method comprises identifying the presence of inflammation and/or inflammatory disease in the subject. In various embodiments, wherein where the proportion of $CD5^-$, $CD14^+$, $CD163^+$, $CD14^+CD163^+$ and/or $CD5^-CD14^+CD163^+$ dendritic cells in the sample is greater than the proportion in an earlier sample from the same subject, the method comprises identifying a worsening of inflammation and/or inflammatory disease in the subject. In various embodiments, wherein where the proportion of $CD5^-$, $CD14^+$, $CD163^+$, and/or $CD14^+CD163^+$ dendritic cells in the sample is lower than the proportion in the earlier sample, the method comprises identifying an improvement of inflammation and/or inflammatory disease in the subject.

In some embodiments, there is provided a method for diagnosing an inflammatory disease in a subject in need thereof, the method comprising: determining and/or detecting and/or quantifying a level or a proportion of a dendritic cell expressing CD5, CD14 and/or CD163 in a sample obtained from the subject; wherein an increased level or proportion of the dendritic cell expressing CD163 and/or CD14, and/or a decreased/reduced level or proportion of the dendritic cell expressing CD5 as compared to a control subject is indicative of the subject having the inflammatory disease. In some embodiments, an increased level or an increased proportion of $CD5^-$, $CD14^+$, $CD163^+$, $CD14^+CD163^+$ and/or $CD5^-CD14^+CD163^+$ dendritic cells as compared to a control subject is indicative of the subject having the inflammatory disease. As used herein, the terms "diagnosing", "diagnosed", and "diagnose" refer to determining the presence and/or absence of a disease or condition based upon an evaluation of physical signs, symptoms, history, laboratory test results, and/or procedures. It would be understood that the final "diagnosing" would ultimately be performed by a

qualified medical profession and that the method as disclosed herein merely provides an assistance to the qualified medical profession in providing the diagnosis. Thus, the methods as disclosed herein cannot be construed to be replacing the function of a qualified medical profession. As used herein, the term "an increased level" refers to the number of cells and/or the level of a protein expression and/or gene transcription and/or other related biomarkers in a sample (biological sample) obtained from the subject which is greater than the number of cells and/or level of protein expression and/or gene transcription and/or other related biomarkers in a control. As used herein, the term "a decreased level" or "a reduced level" refers to the number of cells and/or the level of a protein expression and/or gene transcription and/or other related biomarkers in a sample (biological sample) obtained from the subject which is greater than the number of cells and/or level of protein expression and/or gene transcription and/or other related biomarkers in a control. As used herein, the term "detecting" or "detection" means any of a variety of methods known in the art for determining the presence of a nucleic acid or a protein or a cell. In some examples, to detect a cell of interest, an antibody that is either directly or indirectly labelled can be used to bind the cell of interest and/or a protein expressed on the cell of interest. In some examples, to detect a nucleic acid sequence of interest, a portion of the nucleic acid of interest can be detected by hybridizing a labelled probe to the portion of the nucleic acid. In some examples, to detect a protein of interest, an antibody that is either directly or indirectly labelled can be used to bind to the protein of interest. Methods for labelling nucleic acid and/or antibodies (or other proteins capable of binding to a target of interest) are well known in the art. Labels can be either detectable or functional labels, and include radio-isotope label (such as ^{131}I, ^{125}I, ^{35}S, and ^{99}Tc), enzymatic labels (such as horseradish peroxidase, alkaline phosphatase, and the like), chemiluminescent labels, and other chemical moieties (such as biotin). It is also envisaged that the term "detecting" as used herein includes either qualitative or quantitative detection. Advantageously, embodiments of the method may be implemented as a diagnostic tool.

In various embodiments, the control subject is a person and/or a population of general public who is/are not suffering from the

disease/disorder/condition. In various embodiments, the control sample is a sample obtained from a person and/or a population of general public who is/are not suffering from the disease/disorder/condition. A control sample may also be a healthy or undiseased sample, e.g. a healthy or undiseased paired sample, obtained from the subject.

In various embodiments, the inflammatory disease is selected from the group consisting of systemic inflammatory disease, metabolic disorder, autoimmune disease and cancer.

In various embodiments, the inflammatory disease is selected from the group consisting of inflammatory skin disease, inflammatory bowel diseases, asthma, acute respiratory distress syndrome, chronic obstructive pulmonary disease, acute lung injury, bronchopulmonary dysplasia, cystic fibrosis, bronchitis, bronchiolitis, arthritis, osteoarthritis, ankylosing spondylitis and rheumatism.

In various embodiments, the metabolic disorder is selected from the group consisting of obesity, diabetes (for example diabetes type II, gestational diabetes, MODY) satiety and endocrine deficiencies related to aging.

As used herein, the term "metabolic disorder" refers to any pathological condition resulting from an alteration in a subject's metabolism. For example, a metabolic disorder may result from an alteration in glucose homeostasis resulting in hyperglycaemia.

In various embodiments, the autoimmune disease comprises a systemic autoimmune disease.

In various embodiments, the autoimmune disease is selected from the group consisting of Systemic Lupus Erythematosus (SLE), diabetes, rheumatoid arthritis (RA), multiple sclerosis (MS), myasthenia gravis (MG), scleroderma, Crohn's disease, ulcerative colitis, Hashimoto's disease, Graves' disease, Sjögren's syndrome, polyendocrine failure, vitiligo, peripheral neuropathy, graft-versus-host disease, autoimmune polyglandular syndrome type I, acute glomerulonephritis, Addison's disease, adult-onset idiopathic hypoparathyroidism (AOIH), alopecia totalis, amyotrophic lateral sclerosis, ankylosing spondylitis, autoimmune aplastic anemia, autoimmune hemolytic anemia, Behcet's disease,

Celiac disease, chronic active hepatitis, CREST syndrome, dermatomyositis, dilated cardiomyopathy, eosinophilia-myalgia syndrome, epidermolisis bullosa acquisita (EBA), giant cell arteritis, Goodpasture's syndrome, Guillain-Barré syndrome, hemochromatosis, Henoch-Schönlein purpura, idiopathic IgA nephropathy, insulin-dependent diabetes mellitus (IDDM), juvenile rheumatoid arthritis, Lambert-Eaton syndrome, linear IgA dermatosis, myocarditis, narcolepsy, necrotizing vasculitis, neonatal lupus syndrome (NLE), nephrotic syndrome, pemphigoid, pemphigus, polymyositis, primary sclerosing cholangitis, psoriasis, atopic dermatitis, rapidly-progressive glomerulonephritis (RPGN), Reiter's syndrome, stiff-man syndrome and thyroiditis.

In some embodiments, the autoimmune disease is selected from the group consisting of psoriasis, atopic dermatitis, Systemic Lupus Erythematosus (SLE) and systemic sclerosis (SSc).

As used herein, “autoimmune disease” refers to those disease states and conditions wherein the immune response of the subject is directed against the subject’s own constituents, resulting in an undesirable and often debilitating condition. “Autoimmune disease” is intended to further include autoimmune conditions, syndromes, and the like.

In various embodiments, the cancer comprises a non-solid tumour, optionally wherein the non-solid tumor is selected from the group consisting of leukaemia, multiple myelomas and lymphomas.

In various embodiments, the cancer comprises a solid tumor, optionally wherein the solid tumour comprises sarcoma and/or carcinoma, further optionally wherein the sarcoma and/or carcinoma is selected from the group consisting of hepatocellular carcinoma, fibrosarcoma, myxosarcoma, liposarcoma, chondrosarcoma, osteogenic sarcoma, chordoma, angiosarcoma, endotheliosarcoma, lymphangiosarcoma, lymphangioendotheliosarcoma, synovioma, mesothelioma, Ewing's tumor, leiomyosarcoma, rhabdomyosarcoma, colon carcinoma, pancreatic cancer, breast cancer, ovarian cancer, prostate cancer, squamous cell carcinoma, basal cell carcinoma, adenocarcinoma, sweat gland carcinoma, sebaceous gland carcinoma, papillary carcinoma, papillary adenocarcinomas, cystadenocarcinoma, medullary

carcinoma, bronchogenic carcinoma, renal cell carcinoma, hepatoma, bile duct carcinoma, choriocarcinoma, seminoma, embryonal carcinoma, Wilms' tumor, cervical cancer, testicular tumor, lung carcinoma, small cell lung carcinoma, bladder carcinoma, epithelial carcinoma, glioma, astrocytoma, medulloblastoma, craniopharyngioma, ependymoma, pinealoma, hemangioblastoma, acoustic neuroma, oligodendroglioma, meningioma, melanoma, neuroblastoma, and retinoblastoma.

In some embodiments, the cancer is selected from the group consisting of hepatocellular carcinoma, follicular lymphoma, small lymphocytic lymphoma, pancreatic tumour and breast cancer.

In various embodiments, the method further includes a step of treating the subject with a modulatory agent and/or an inhibitory agent and/or a depleting agent to reduce the level or proportion of the dendritic cells expressing CD163 and/or CD14, and/or the level or proportion of the $CD5^-$, $CD14^+$, $CD163^+$, $CD14^+CD163^+$ and/or $CD5^-CD14^+CD163^+$ dendritic cells. As used herein, the term "modulatory agent" refers to any compound, molecule or substance capable of "modulating" dendritic cell gene expression at the transcriptional, translational, or post-translational levels or modulating the biological activity of a dendritic cell population of interest or removing (or reducing the total number) the dendritic cell population of interest. The term "modulate" and its cognates refer to the capability of a compound/molecule/substance acting as either an agonist or an antagonist of a certain reaction or activity. The term “modulate”, therefore, encompasses the terms "activate" and "inhibit." The term "activate" or “increase” for example, refers to an increase in the expression of the dendritic cell (such as DC3) gene or activity of a dendritic cell (such as DC3) secretions (such as chemokines, cytokines, and the like) or increase in the number of dendritic cell in the presence of a modulatory compound, relative to the activity of the gene or the polypeptide in the absence of the same compound. The increase in the expression level or the activity or total number of dendritic cells may be at least about 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, or higher. Analogously, the term "inhibit" or “reduce” refers to a decrease in the expression of the dendritic cell (such as DC3) gene or activity of the dendritic cell (such as DC3) polypeptide or decreased in total number of

dendritic cells in the presence of a modulatory compound, relative to the activity of the gene or the polypeptide or total number of cells in the absence of the same agent/compound/molecule. The decrease in the expression level or the activity or total cell number may be at least about 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, or higher. The expression level of the dendritic cell (such as DC3) gene or activity or total number of the dendritic cell (such as DC3) can be measured as described herein or by techniques generally known in the art.

In various embodiments, wherein where the presence and/or the worsening of inflammation and/or an inflammatory disease in the subject is identified, the method further comprises allocating the subject to an inflammation and/or an inflammatory disease treatment regimen.

In various embodiments, the inflammation and/or inflammatory disease treatment regimen comprises administering to the subject a modulatory agent and/or an inhibitory agent and/or a depleting agent to reduce the level or proportion of the dendritic cells expressing CD163 and/or CD14, and/or the level or proportion of the $CD5^-$, $CD14^+$, $CD163^+$, $CD14^+CD163^+$, $CD5^-CD163^-$, $CD5^-CD163^+CD14^-$ and/or $CD5^-CD163^+CD14^+$ dendritic cells. In various embodiments, the inflammation and/or inflammatory disease treatment regimen comprises administering to the subject one or more agent selected from the group consisting of: an anti-inflammatory agent, an immunosuppressant agent, an anti-cancer agent, an inhibitor of FLT3L, an agent capable of binding to $CD5^-$, $CD14^+$, $CD163^+$, $CD14^+CD163^+$, $CD5^-CD163^-$, $CD5^-CD163^+CD14^-$ and/or $CD5^-CD163^+CD14^+$ dendritic cells, an agent capable of neutralising $CD5^-$, $CD14^+$, $CD163^+$, $CD14^+CD163^+$, $CD5^-CD163^-$, $CD5^-CD163^+CD14^-$ and/or $CD5^-CD163^+CD14^+$ dendritic cells, an antibody against $CD5^-$, $CD14^+$, $CD163^+$, $CD14^+CD163^+$, $CD5^-CD163^-$, $CD5^-CD163^+CD14^-$ and/or $CD5^-CD163^+CD14^+$ dendritic cells, an agent capable of reducing the proportion of $CD5^-$, $CD14^+$, $CD163^+$, $CD14^+CD163^+$, $CD5^-CD163^-$, $CD5^-CD163^+CD14^-$ and/or $CD5^-CD163^+CD14^+$ dendritic cells, an agent capable of reducing an activity of $CD5^-$, $CD14^+$, $CD163^+$, $CD14^+CD163^+$, $CD5^-CD163^-$, $CD5^-CD163^+CD14^-$ and/or $CD5^-CD163^+CD14^+$ dendritic cells, an agent capable of reducing a number of a precursor of $CD5^-$, $CD14^+$, $CD163^+$, $CD14^+CD163^+$, $CD5^-CD163^-$, $CD5^-$

$CD163^+CD14^-$ and/or $CD5^-CD163^+CD14^+$ dendritic cells and an agent capable of inhibiting a differentiation of the precursor of $CD5^-$, $CD14^+$, $CD163^+$, $CD14^+CD163^+$, $CD5^-CD163^-$, $CD5^-CD163^+CD14^-$ and/or $CD5^-CD163^+CD14^+$ dendritic cells.

In one embodiment, the treatment regimen comprises administering to the subject an inhibitor of FLT3L.

In one embodiment, the treatment regimen comprises contacting the sample to an agent capable of binding and/or neutralising the dendritic cells expressing CD163 and/or CD14 and/or binding and/or neutralising $CD5^-$, $CD14^+$, $CD163^+$, $CD14^+CD163^+$, $CD5^-CD163^-$, $CD5^-CD163^+CD14^-$ and/or $CD5^-CD163^+CD14^+$ dendritic cells. In some examples, the agent capable of binding and/or neutralising the dendritic cells is an antibody. In some embodiments, therefore, the treatment regimen comprises administering to the subject an antibody capable of specifically binding to the dendritic cells expressing CD163 and/or CD14, and/or $CD5^-$, $CD14^+$, $CD163^+$, $CD14^+CD163^+$, $CD5^-CD163^-$, $CD5^-CD163^+CD14^-$ and/or $CD5^-CD163^+CD14^+$ dendritic cells. As used herein, the term "antibody" refers to an immunoglobulin or fragment thereof, and encompasses any polypeptide comprising an antigen-binding fragment or an antigen-binding domain. The term includes but is not limited to polyclonal, monoclonal, monospecific, polyspecific (such as bi-specific), humanized, human, single-chain, chimeric, synthetic, recombinant, hybrid, mutated, grafted, and *in vitro* generated antibodies. The term "antibody" may include antibody fragments such as Fab, $F(ab')_2$, Fv, scFv, Fd, dAb, and other antibody fragments that retain antigen-binding function. An antibody is not necessarily from any particular source, nor is it produced by any particular method.

In one embodiment, the treatment regimen comprises administering an agent capable of removing and/or depleting a precursor of dendritic cells expressing CD163 and/or CD14, and/or a precursor of $CD5^-$, $CD14^+$, $CD163^+$, $CD14^+CD163^+$, $CD5^-CD163^-$, $CD5^-CD163^+CD14^-$ and/or $CD5^-CD163^+CD14^+$ dendritic cells. In various embodiments, the precursor comprises a dendritic precursor cell expressing CD5. In various embodiments, the precursor has one or more of the following expression or phenotype: $CD56^+$, $CD303^+$, $CD271^+$,

$CD22^+$, $CD124^+$, $CD324^+$, integrin $\beta7^+$, $BTLA^+$, $CD26^+$, $CD183^+$, $CD71^-$, $CD59^-$, $CD218a^+$, $CD200^+$, $CD195^+$, $CD1c^+$, $CD282^-$, $CD107a^-$, $CD11b^-$, $CD274^+$, $CD14^+$, $CD166^+$, $CD81^-$, $CLEC12A^-$, $CD63^-$, $CD84^-$, $CD115^-$, $CD95^-$, $CD163^-$, $CD34^{int}$, $CD112^-$, $CD155^-$, $CD206^-$, $CD172a^-$, $CD354^-$, $CD36^-$, Igk^-, $CD64^-$, and $CD87^-$. In various embodiments, the precursor further expresses one or more nucleic acids/genes/proteins/markers selected from the group consisting of nucleic acids/genes/proteins/markers related to integrin signalling, FcγR-mediated phagocytosis, VEGF signalling, EIF2 signalling, leukocyte extravasation signalling, IL-3 signalling, Fc Epsilon RI signalling, mTOR signalling, IL-6 signalling, antigen presentation pathway, chemokine signalling, GM-CSF signalling, Tec Kinase signalling, FLT3 signalling in HPCs, NF-κB activation by viruses, IL-12 signalling and production in macrophages, and the like. In some examples, the genes expressed by the precursor of the dendritic cell expressing CD163 is listed in FIG. 10D and FIG. 10G. In various embodiments, the precursor expresses one or more nucleic acids/genes/proteins/markers selected from the group consisting of CD74, AXL, CD207, SIGLEC6, CD5, and BTLA.

In various embodiments, dendritic cells expressing CD5 (e.g. $CD5^+DC2$) are precursors to dendritic cells that do not express or minimally express CD5 (e.g. $CD5^-$ DC3). Thus, blockage of $CD5^+$ precursors to $CD5^-$ dendritic cells differentiation and/or activation can be a therapeutic strategy for inflammatory diseases.

In various embodiments, the method further comprises determining a prognosis of the inflammation and/or inflammatory disease in the subject by measuring the level and/or the proportion of the dendritic cells expressing CD163 and/or CD14, and/or the level and/or the proportion of $CD5^-$, $CD14^+$, $CD163^+$, $CD14^+CD163^+$, $CD5^-CD163^-$, $CD5^-CD163^+CD14^-$ and/or $CD5^-CD163^+CD14^+$ dendritic cells in a sample obtained from the subject after the subject has received the treatment regimen. As used herein, the term “prognosis” refers to the prediction of the likelihood of disease-attributable progression, including increased in severity or death, metastatic spread (of cancer), drug resistance (of cancer), or reversal, including reduction in severity or complete remission (from cancer).

Advantageously, embodiments of the method may be used for the identification, quantification and subsequent targeting of a body response such as inflammation and/or a disease such as an inflammatory disease.

In various embodiments, the method of characterising dendritic cells may also be relevant to a method of treating a body response such as inflammation and/or a disease such as an inflammatory disease in a subject, a method of assessing the extent/severity of a body response such as inflammation and/or a disease such as an inflammatory disease in a subject, a method of assessing the prognosis of a body response such as inflammation and/or a disease such as an inflammatory disease in a subject and the like.

In various embodiments, there is provided a method of treating inflammation and/or inflammatory disease in a subject, the method comprising administering to the subject an agent and/or a treatment regimen as described herein. In some embodiments, the method comprises administering to the subject an agent capable of modulating the level and/or the proportion of the dendritic cells expressing CD163 and/or CD14, and/or the level and/or the proportion of $CD5^-$, $CD14^+$, $CD163^+$, $CD14^+CD163^+$, $CD5^-CD163^-$, $CD5^-CD163^+CD14^-$ and/or $CD5^-CD163^+CD14^+$ dendritic cells. In various embodiments, the method further comprises determining a level and/or a proportion of the dendritic cells expressing CD163 and/or CD14, and/or a level and/or a proportion of $CD5^-$, $CD14^+$, $CD163^+$, $CD14^+CD163^+$, $CD5^-CD163^-$, $CD5^-CD163^+CD14^-$ and/or $CD5^-CD163^+CD14^+$ dendritic cells in a sample obtained from the subject. In various embodiments, the subject has or is determined to have an increased level and/or proportion of the dendritic cells expressing CD163 and/or CD14, and/or an increased level and/or proportion of $CD5^-$, $CD14^+$, $CD163^+$, $CD14^+CD163^+$, $CD5^-CD163^-$, $CD5^-CD163^+CD14^-$ and/or $CD5^-CD163^+CD14^+$ dendritic cells in his/her sample as compared to a control sample or a sample obtained from a control subject.

In various embodiments, there is provided a method of assessing the severity of an inflammatory disease in a subject, the method comprising determining a level and/or a proportion of the dendritic cells expressing CD163 and/or CD14, and/or a level and/or a proportion of $CD5^-$, $CD14^+$, $CD163^+$, $CD14^+CD163^+$, $CD5^-CD163^-$, $CD5^-CD163^+CD14^-$ and/or $CD5^-CD163^+CD14^+$

dendritic cells in a sample obtained from the subject. In various embodiments, an increased level and/or a proportion of the dendritic cells expressing CD163 and/or CD14, and/or an increased level and/or a proportion of $CD5^-$, $CD14^+$, $CD163^+$, $CD14^+CD163^+$, $CD5^-CD163^-$, $CD5^-CD163^+CD14^-$ and/or $CD5^-CD163^+CD14^+$ dendritic cells in the sample is correlated (e.g. positively correlated)/indicative of the severity of the inflammatory disease in the subject. In one embodiment, the method comprises a method of assessing the severity of a Systemic Lupus Erythematosus (SLE).

In various embodiments therefore, there is provided a method of assessing the severity of Systemic Lupus Erythematosus (SLE) in a subject, the method comprising determining a level and/or a proportion of the dendritic cells expressing CD163 and/or CD14, and/or a level and/or a proportion of $CD5^-$, $CD14^+$, $CD163^+$, $CD14^+CD163^+$, $CD5^-CD163^-$, $CD5^-CD163^+CD14^-$ and/or $CD5^-CD163^+CD14^+$ dendritic cells in a sample obtained from the subject. In various embodiments, an increased level and/or a proportion of the dendritic cells expressing CD163 and/or CD14, and/or an increased level and/or a proportion of $CD5^-$, $CD14^+$, $CD163^+$, $CD14^+CD163^+$, $CD5^-CD163^-$, $CD5^-CD163^+CD14^-$ and/or $CD5^-CD163^+CD14^+$ dendritic cells in the sample is correlated (e.g. positively correlated)/indicative of the severity of the SLE in the subject. For example, a subject with an increased level and/or a proportion of the dendritic cells expressing CD163 and/or CD14, and/or an increased level and/or a proportion of $CD5^-$, $CD14^+$, $CD163^+$, $CD14^+CD163^+$, $CD5^-CD163^-$, $CD5^-CD163^+CD14^-$ and/or $CD5^-CD163^+CD14^+$ dendritic cells in his/her sample may have a higher SLE Disease Activity Index (SLEDAI) score (i.e. having a more significant degree of disease activity). In some examples, dendritic cells (e.g. DC3) expressing CD163 molecule are found to be increased in SLE patients in correlation with the gravity of the disease as determined by the SLEDAI score. Advantageously, the level or the proportion of dendritic cells, e.g. pro-inflammatory dendritic cells, may be quantified by flow cytometry and be used to predict the disease score in patients with SLE. In various embodiments, the method further comprises administering to the subject a SLE treatment regimen. In various embodiments, the SLE treatment regimen comprises administering to the subject an agent that is

capable of decreasing the activity of the dendritic cell expressing CD163 by decreasing/inhibiting the secretion of pro-inflammatory mediators involved in SLE physiopathology such as, but is not limited to, BAFF, IL-1α, GRO-α (CXCL1), MCP-3 (CCL7), MIG (CXCL9), SDF-1 (CDCL12), IL-8, VEGF-A, and WEAK.

In various embodiments, there is provided a method of assessing the prognosis of an inflammatory disease in a subject, the method comprising determining a level and/or a proportion of the dendritic cells expressing CD163 and/or CD14, and/or a level and/or a proportion of $CD5^-$, $CD14^+$, $CD163^+$, $CD14^+CD163^+$, $CD5^-CD163^-$, $CD5^-CD163^+CD14^-$ and/or $CD5^-CD163^+CD14^+$ dendritic cells in a sample obtained from the subject. In various embodiments, a decreased level and/or a proportion of the dendritic cells expressing CD163 and/or CD14, and/or an decreased level and/or a proportion of $CD5^-$, $CD14^+$, $CD163^+$, $CD14^+CD163^+$, $CD5^-CD163^-$, $CD5^-CD163^+CD14^-$ and/or $CD5^-CD163^+CD14^+$ dendritic cells in the sample is correlated (e.g. positively correlated)/indicative of prognosis/improvement of the inflammatory disease in the subject.

In various embodiments, the sample (or biological sample) is a fluid or specimen from a person/patient/subject such as whole blood, serum, plasma, tears, saliva, nasal fluid, sputum, ear fluid, genital fluid, breast fluid, milk, colostrum, placental fluid, amniotic fluid, stool, perspirate, synovial fluid, ascites fluid, cerebrospinal fluid, bile, gastric fluid, aqueous humor, vitreous humor, gastrointestinal fluid, exudate, transudate, pleural fluid, pericardial fluid, semen, upper airway fluid, peritoneal fluid, fluid harvested from a site of an immune response, fluid harvested from a pooled collection site, bronchial lavage, urine, biopsy material, e.g. from all suitable organs, e.g. the lung, the muscle, brain, liver, skin, pancreas, stomach, etc., a nucleated cell sample, a fluid associated with a mucosal surface, hair, or skin. In some examples, the sample may be blood (whole blood), serum, plasma, biological fluid, tissue biopsies, sputum, interstitial fluid, and the like.

In various embodiments, the sample comprises human biological material. In various embodiments, the sample comprises MNP. In various embodiments, the sample comprises a MNP subpopulation. In various embodiments, the

sample comprises one or more of dendritic cells, monocytes, macrophages and monocyte-derived cells (MC). In one embodiment, the sample comprises dendritic cells. In one embodiment, the sample comprises cDC2. In one embodiment, the sample comprises dendritic cells having one or more of the following properties: (i) is a conventional dendritic cell 2 (cDC2); (ii) is dependent on IRF4 for differentiation; (iii) is dependent on KLF4 for differentiation; (iv) is dependent on FLT3 ligand (FLT3L) for differentiation; and (v) is capable of activating and/or polarizing T cells e.g. naïve T cells or allogeneic naïve CD4+ T cells.

In various embodiments, there is provided a kit for use in the methods described herein. In various embodiments, the kit comprises one or more reagents for detecting/determining/quantifying a dendritic cell expressing CD163 and/or CD14, and/or a level and/or a proportion of $CD5^-$, $CD14^+$, $CD163^+$, $CD14^+CD163^+$, $CD5^-CD163^-$, $CD5^-CD163^+CD14^-$ and/or $CD5^-CD163^+CD14^+$ dendritic cells. In various embodiments, there is provided a kit for characterising dendritic cells, inflammation and/or inflammatory disease, the kit comprising one or more reagent for detecting/determining/quantifying CD5, CD14 and/or CD163. In various embodiments. In some embodiments, the kit comprises one or more of an anti-CD5 antibody, an anti-CD14 antibody and/or an anti-CD163 antibody.

In various embodiments, the kit further comprises one or more reagent for detecting/determining/quantifying AXL, BLTA, BTLA, CD101, CD107a, CD109, CD112, CD115, CD11b, CD124, CD14, CD155, CD163, CD166, CD172a, CD180, CD183, CD195, CD1c, CD1d, CD2, CD200, CD200R, CD206, CD218a, CD22, CD229, CD26, CD271, CD274, CD282, CD303, CD324, CD34, CD354, CD36, CD45RA, CD5, CD56, CD59, CD63, CD64, CD71, CD74, CD81, CD84, CD87, CD87 , CD88, CD89, CD95, CLEC12A, CLEC4E, DNAI2, FcεRIα , HLA-DQ, Igk, Integrin β7, LTB (Lymphotoxin-b), MEX3B, NOTCH2, NUMBL, RN7SL846P, S100A13, S100A8, S100A9, S100A9, SIGLEC6 (CD327). In some embodiments, the kit comprises one or more reagent for detecting/determining/quantifying AXL, BLTA, CD1c, CD1d, CD5, CD11b, CD64, CD74, CD88, CD89, CD101, CD109, CD180, CD200R, CD45RA, FcεRIα HLA-DQ, Integrin β7, LTB (Lymphotoxin-β), NOTCH2, S100A8, S100A9 and SIGLEC6

(CD327). In some embodiments, the kit comprises one or more reagent for detecting/determining/quantifying CD5, CD163, CD14, CD11b, CD36, CD64, CD87, CD107a, CD206, CD274, CD354, FcεRIα, HLA-DQ, CD2, CD59, CD81, CD166, CD229, CD271 and Integrin β7.

In various embodiments, there is provided a population, e.g. an isolated population, of dendritic cells selected from the group consisting of: $CD5^-$ dendritic cells, $CD14^+$ dendritic cells, $CD163^+$ dendritic cells, $CD14^+CD163^+$ dendritic cells, $CD5^-CD163^-$ dendritic cells, $CD5^-CD163^+CD14^-$ dendritic cells and/or $CD5^-CD163^+CD14^+$ dendritic cells. The term "isolated" as used herein in relation to a population of cells refers to a population of cells that is removed from its natural environment (e.g. tissue, body fluid, etc.), or otherwise increased in purity to any degree. A population may be "isolated" by separating it from some or all of the substances with which it is associated in nature. In various embodiments, the isolated population is substantially pure and/or homogenous (e.g. substantially free/devoid of dendritic cells having other expression profiles and/or phenotypes, and/or substantially free/devoid of other impurities and/or contaminants).

In various embodiments, there is provided a method, a kit, a reagent, a compound, or an agent as described herein.

BRIEF DESCRIPTION OF FIGURES

FIG. 1. InfinityFlow, a high-dimensional single-cell protein expression pipeline, unravels human circulating myeloid cell phenotypes and heterogeneity. (**A**) Peripheral blood mononuclear cells from a single donor were stained with 14 back-bone markers, divided, stained with 332 PE-conjugated variable antibodies (LegendScreen kit) and then analyzed by flow cytometry. The 332 generated fcs files were analyzed with the InfinityFlow pipeline to generate fcs files containing 347 dimensions, consisting of 14 back-bone dimensions, 1 variable-PE real marker and 332 predicted markers. (**B**) tSNE dimensionality reduction and Phenograph clustering of $CD45^+CD3^-CD20^-HLA\text{-}DR^+$ peripheral blood (PB) mononuclear phagocytes (MNP) based on the 332 predicted dimensions. Cell subsets were delineated using the 23 Phenograph

clusters (pDC, n=2 clusters; pre-DC, n=1 cluster; cDC1, n=1 cluster; cDC2, n=4 clusters; cMo, n=8 clusters; iMo, n=2 clusters; ncMo, n=3 clusters; contaminating B cells and $CD34^+$ cells, n= 1 cluster each; one minor undetermined cluster representing 1.1% of cells) that were regrouped into major previously defined cell subsets based on the expression of cell-subset specific phenotypic markers. (**C**) Expression heatmap of makers highly expressed by the different monocyte and DC subsets. Newly defined cell subset discriminating markers are indicated in grey. (**D**) tSNE dimensionality reduction and Phenograph clustering of $CD45^+CD3^-CD20^-HLA\text{-}DR^+$ PB MNPs based on the 92 discriminating markers defined in FIG. 1C.

FIG. 2. (**A**) Gating strategy of flow cytometry data starting from singlet, live, $CD45^+$ cells, for the export of $Lin^-HLA\text{-}DR^+$ cells analyzed with the InfinityFlow pipeline. (**B**) Meaning plots of the relative expression of backbone markers and their respective predicted dimensions in the 332 dimensions tSNE from FIG. 1B. (**C**) Heat map of the 332 predicted dimensions clustered by Euclidean distance for cell subsets defined in FIG. 1B-C. Markers that were highly expressed only by one of the 7 major cell types analysed (within the black rectangles) were defined as "discriminating markers" and displayed in FIG. 1C. (**D**) Meaning plots of the relative expression of backbone makers and their respective predicted dimensions in the discriminating markers tSNE from FIG. 1D. (**B**,**D**) Predicted "variable PE" dimensions were obtained by a regression-based approach integrating the expression of backbone markers (measured in each of the 332 FACS stainings).

FIG. 3. (**A**) Histograms showing the expression of highly expressed markers by all cell subsets defined in FIG. 1B-C. (**B**) Histograms showing the expression of markers over-expressed by pre-cDC2 to cDC2 and early pre-DC, as defined by See *et al.* (See et al., 2017). Expression is also compared to cDC1 and pDC.

FIG. 4. $CD1c^+CD14^+$ circulating cells are phenotypically and functionally related to cDC2 and not monocytes. (**A**) cDC2 and cMo Phenograph clusters represented in the tSNE generated using the 92 markers described in FIG. 1D, and in a CD14/CD1c dot plot. (**B**) cMo versus cDC2

Phenograph clusters were compared by AUC analysis to determine their discriminating markers. (**C**) Relative expression of the classical and top four discriminating markers of cDC2 and cMo (real dimensions displayed). (**D**) Optimal gating strategy starting from $Lin^-HLA\text{-}DR^+$ defining all blood MNP subsets. (**E**) UMAP analysis of data from panel (**D**). (**F**) Phenotype of cells within cDC2 (grey) and monocyte (black) defined in the UMAP space. (**G-I**) Human blood, spleen and tonsil were analyzed by CyTOF using the new cMo/cDC2 discriminating markers. Among $Lin^-HLA\text{-}DR^+$ cells (concatenated data), (**G**) the relative expression of MNP subsets-defining markers and (**H**) distribution of cells from the three tissues are shown. (**I**) Differentially expressed markers between tissues. (**J-K**) The relative proportions of cMo, $CD1c^+CD14^-$ and $CD1c^+CD14^+$ cDC2 were measured in the blood of seven patients before and 11 days after FLT3L treatment. (**K**) Proportions of subsets and (**L**) Relative expression of IRF4, KLF4 and NOTCH2 for the cell subsets defined in (**J**).

FIG. 5. (**A**) Markers with an AUC <0.1 and >0.9. (**B**) Meaning plots of the relative expression of CD1c, CD14, FcεRIα, HLA-DQ, CD88 and CD89 markers showing real dimensions and their respective predicted dimensions on the tSNE using the discriminating markers defined in FIG. 1C. (**C**) Meaning plots of the relative expression of other cDC2 and cMo discriminating markers. (**D**) Flow cytometry dot plot of CD14 versus discriminating markers between cDC2 and cMo. (**E**) Manual gating strategy from Hamers et al. to define 8 monocyte subsets (Hamers Anouk A.J. et al., 2019). The cell subsets were back-gated in the mother gates of the gating strategy. (**F**) Projection of the 8 monocyte subsets defined in (**A**) into the tSNE obtained using the 332-predicted dimensions of the InfinityFlow data (see FIG. 1B of our manuscript). (**G**) Gating strategy of flow cytometry data starting from singlet, live, $CD45^+$ cells, for the export of $CD163^+$ cells falling between cDC2 and cMo. (**H**) PCA using the 14 backbone markers of cells exported in (**G**). Meaning plots showing the relative expression of CD1c, CD163 and CD14 real dimensions and the 40 binning gates. (**I**) tSNE/Phenograph analysis using the 332 predicted dimensions (PE markers) for the 40 bins defined in (**H**). (**J**) Dot plots showing the expression of CD14, CD1c (real dimensions), PC1 and PC4 of cells falling in the Phenograph clusters defined in (**I**). (**K**)

Meaning plots of the relative expression of all makers used in the flow cytometry analysis of FIG. 4E-F. (**L**) Meaning plots of the relative expression of selected makers used in the CyTOF analysis of FIG. 4G-H. (**M-N**) Expression heatmap of markers with a higher expression in (**M**) (cDC2) and (**N**) (monocyte/macrophages). (**O**) Histograms showing the expression of markers selected as being differentially expressed between tissues (the median expression intensity values are shown). (**P**) Gating strategy starting from singlet, live, $CD45^+$ cells from FLT3L-injected patients analyzed in FIG. 4J-K.

FIG. 6. (**A-B**) Gating strategy of the flow cytometry data from (**A**) the full recording and (**B**) indexed-sorted cells analyzed by SMARTseq2 scRNAseq of FIG. 7. (**C**) Meaning plots of the relative expression of selected flow cytometry markers from the tSNE analysis of FIG. 7A. (**D-E**) In the tSNE analysis of FIG. 7A, (**D**) cells that did or did not pass quality control for SMARTseq2 analysis are displayed in black or dark grey, respectively (numbers of total indexed-sorted cell, of cells that passed QC and their frequencies indicated), and (**E**) cell subsets defined in FIG. 7E-F are displayed. (**F** and **G**) From the scRNAseq data of FIG. 7B-C, visualizations are presented of UMAP and (**F**) Phenograph clusters or (**G**) cell subsets defined based on the indexed-protein expression in FIG. 7E-F. (**H**) Meaning plots of the relative expression of top signature genes in the DC subsets described by Villani *et al.* (Villani et al., 2017). (**I**) Meaning plots of the relative expression of specific, highly expressed genes (signature genes) by cDC2 clusters #2 and #4 defined by comparing them to all other cells. (**J**) Conventional flow cytometry gating strategy to define AS-DC (DC5, upper panel; light grey) and early pre-DC (lower panel; dark grey) from Villani *et al.* and See *et al.*, respectively (See et al., 2017; Villani et al., 2017). (**K**) Density plots showing the expression of CD11c, CD1c, CD169, CD45RA and CD123 by AS-DC (light grey) and early pre-DC (dark grey). (**L**) Volcano plots comparing the expression of genes between cDC2 clusters #2 and #4 (defined in FIG. 7B-C) represented as the mean Log2(Fold Change) vs -Log10(adjusted p value). (**M**) Ingenuity pathway analysis (IPA) of cDC2 clusters #2 versus #4 DEG. The histogram height represents the -log(p value), and the proportion of DEG from each pathway up-regulated in cDC2 clusters #2 (dark grey) and #4 (light grey) is shown. Significant

pathways obtained when including only the upregulated genes in cDC2 clusters #2 or #4 (IPA) are marked by a dark grey or a light grey star, respectively.

FIG. 7. Indexed single-cell RNAseq analysis confirms that CD1c$^+$CD14$^+$ circulating cells are inflammatory cDC2 and not monocytes. (**A**) tSNE of indexed-sorted DC subsets and monocytes (black dots) overlayed on Lin$^-$HLA-DR+ PBMCs (full recording). (**B-H**) Indexed-sorted cells were analyzed by scRNAseq using the Seurat pipeline and phenograph clustering. (**B-C**) For the eight phenograph clusters, (**B**) the heatmap of the top 20 DEG and (**C**) their projection on a tSNE obtained using 10 Seurat significant principal components (PCs; Principal Component Analysis, PCA) identified monocytes, DC subsets and CD16$^{+/-}$HLA-DR^{lo} contaminating NK cells. (**D**) Protein expression of MNP subsets-defining markers obtained from the FACS-indexed data. (**E**) Monocyte and DC subsets were defined based on indexed-protein expression and (**F**) overlaid on the RNA_tSNE defined in (**C**). (**G-H**) DC and monocyte subset signatures from Villani *et al.* (Villani et al., 2017) are shown as (**E**) a heat map of the top 20 signature genes expressed in the eight phenograph clusters [defined in (**B**)], and (**H**) as the mean expression of all signature genes. (**I**) Visualization of the relative expression of top discriminating membrane protein markers of DC and monocyte subsets described by Villani *et al.* (Villani et al., 2017) on the InfinityFlow tSNE generated using the discriminating markers shown in FIG. 1C.

FIG. 8. High-dimensional analyses unravel heterogeneity of circulating cDC2. (**A**) PCA/Phenograph analysis of cDC2 extracted from the discriminating markers' InfinityFlow tSNE (FIG. 1D) using the 332 predicted protein dimensions. (**B**) PC1/PC2 dimensions (%=PC loading) and Phenograph cluster visualization of cDC2. (**C**) Absolute loading of the top six PC1-2 markers. (**D**) 3D visualization of CD5/CD14/CD163 expression by cDC2. (**E**) Expression of heterogeneously expressed markers for the different cDC2 states [CD5$^+$CD163$^-$ (light grey circle) and among CD5$^-$ cells, CD163$^-$ (dark grey circle), CD163$^+$CD14$^-$ (light grey box) and CD163$^+$CD14$^+$ (dark grey box)]. (**F**) Heatmap of discriminating markers between the four cDC2 states. (**G**) Scanning electron microscopy of FACS-sorted cDC2 subsets and CD88$^+$CD89$^+$CD14^{hi}CD16$^-$ classical monocytes. Scale bar, 2µm. (**H**) Forward scatter (FSC-A) and side

scatter (SSC-A) median fluorescence intensity (MFI) of cells defined as $CD5^+$, $CD5^-CD163^-$, $CD163^+CD14^-$, $CD163^+CD14^+$ cDC2 and as $CD88^+CD89^+CD14^+CD16^-$ cMo.

FIG. 9. (**A**) Bimodal plots of PC1 to PC4 dimensions and Phenograph clusters from the analysis of FIG. 8B (% = PC loading). (**B**) Bimodal plots of PC1 and PC2 top six loading markers and Phenograph clusters from the analysis of FIG. 8B-C. (**C**) Meaning plot of the values of PC1 to PC4 overlaid on a dot pot of CD163 and CD5 real dimensions as in FIG. 8D. (**D**) Meaning plots of the relative expression of real dimensions and their respective predicted dimensions for heterogeneously expressed markers in-between the four cDC2 subsets defined in FIG. 8E. (**E**) Manual gating strategy to define DC and cDC2 subsets, starting from singlet, live $CD45^+Lin^-HLA\text{-}DR^+$ cells and after excluding monocytes (based on CD14/CD88 and CD16 expression). (**F**) Expression of markers (real dimensions) showing progression from early pre-DC to pre-cDC2 (as defined in See *et al.*) (See et al., 2017), to $CD5^+$ cDC2 and then to the other cDC2 subsets ordered based on the Wishbone pseudotime analyses shown in (**H**). All of these cell subsets are defined in (**I**). (**G**) Expression of transcription factors by cell subsets defined in (**I**). (**H**) Meaning plots of the relative expression of real dimensions of CD5, CD163 and CD14 overlaid on the UMAP and isoMAP spaces obtained using the top 20 loading markers from the PCA of FIG. 8B. (**I**) Heatmap of the most variable markers along the NBOR pseudotime trajectory, starting from $CD5^+$ cDC2. (**J**) Graphical representation of the progression of CD5, CD163 and CD14 expression by individual cells along the NBOR pseudotime trajectory. (**K**) Wishbone analysis starting from $CD5^+$ cDC2. The wishbone pseudotime dimension is displayed as early (black) to late (white) on a CD163/CD5 dot plot for total cDC2 and on a CD163/CD14 dot pot for $CD5^-$ cDC2. (**L**) DEG between cDC2 and early pre-DC, taken from See *et al.* (See et al., 2017) microarray data. Genes encoding highly expressed proteins by $CD5^+$ cDC2 are highlighted in grey and bold. (**M**) Scanning electron microscopy of cDC2 subsets and $CD88^+CD89^+CD14^{hi}CD16^-$ classical monocytes. Scale bar, 2µm.

FIG. 10. Functional and molecular characterization of inflammatory $CD14^+$ cDC2. (**A**) The relative proportions of the four cDC2 subsets and

$CD88^+CD89^+CD14^+CD16^-$ cMo, were measured in the blood of four patients before and 11 days after FLT3L treatment. The proportion among cDC2+cMo are displayed. (**B-D**) Bulk RNAseq data obtained from FACS-sorted cDC2 subsets. (**B**) Connectivity map (cMAP) analysis showing the degree of enrichment for Villani's DC2 or DC3 signature genes in the four cDC2 subsets. (**C**) UMAP using the first 10 PC (PCA); Circles delineate DC2 ($CD5^+$ cDC2) and DC3 (the three subsets of $CD5^-$ cDC2). (**D**) Heatmap of six selected specifically expressed DEG for each subset. (**E**) Naïve allogenic $CD4^+$ T cells were cultured with the four different cDC2 subsets: frequencies of proliferating, IFNγ (Th1), IL-4 (Th2) or IL-17 (Th17)-producing $CD4^+$ T cells are represented [linked scatter plots (n=4)]. (**F**) In the indexed-scRNAseq data from FIG. 7, mean expression of specifically expressed genes by inflammatory DC (infIDC) defined by Segura *et al.* (Segura et al., 2013) (Table S2) represented as a violin plot and as a meaning plot on the CD1c/CD14 protein expression dot plot defined in FIG. 7E. (**G**) Ingenuity Pathway Analysis of cDC2 subsets bulk RNAseq displayed as a Radar plot showing -Log(p-value) and z-Score for each pathway using upregulated and downregulated DEG of each subset.

FIG. 11. (**A**) UMAP analysis of FLT3L-injecred patients (data from FIG. 10A) the day of the injection (D0) and 11 days post-injection (D11). (**B**) Heatmap of all DEG obtained by comparing bulk RNAseq of the four cDC2 subsets analyzed in FIG. 10B-C. (**C**) Flow cytometry histograms and dot plots showing the CellTrace Violet dye dilution to follow cell proliferation (x-axis) versus intracellular quantification of IFNγ, IL-4 and IL-17 (y-axis) in $CD4^+$ T cells after 6 days of mixed lymphocyte reaction (MLR) with allogenic cDC2 subsets. (**D**) Meaning plots of the relative expression of infIDC markers [defined by Segura *et al.* (Segura et al., 2013)] by cDC2 subsets defined in FIG. 8D-E. (**E**) Venn diagram of the intersection of infIDC versus BDCA-1 [blood cDC2 BDCA-1 cells from Segura *et al.* (Segura et al., 2013)] DEG (Table S2) compared to the four cDC2 subset DEG obtained from bulk the RNAseq shown in FIG. 10B-C.

FIG. 12. $CD5^-CD163^+$ DC3 accumulate in patients with Systemic Lupus Erythematosus (SLE). (**A-D**) PBMCs were isolated from healthy subjects (n=10), and patients with SLE (n=10) or systemic sclerosis (SSC; n=15), and

cDC2 subsets were defined by FACS. (**B**-**C**) The frequency of cDC2 subsets in the three patient groups is shown among (**B**) $CD45^+$ PBMCs and (**C**) total cDC2. (**D**) Pearson correlation of the frequency of $CD163^+$ ($CD14^-$ and $CD14^+$) DC3 versus the SLE disease activity score (SLEDAI) in SLE patients. (**E**) CD163 and CD169 membrane protein expression by cDC2 subsets in healthy subjects and SLE patients. (**F**-**H**) Bulk RNAseq analysis of FACS-sorted cDC2 subsets from healthy subjects and patients with SLE. (**F-G**) For $CD5^+$ DC2 (healthy, n=5; SLE, n=6) and $CD163^+$ DC3 (healthy, n=5; SLE, n=9), (**F**) an expression heatmap of the top 100 DEG and (**G**) volcano plots showing Log2(Fold Change) vs -Log10(p-value) of all gene expression data comparing healthy and SLE patients are shown. (**H**) Ingenuity Pathway Analysis of $CD5^+$ DC2 and $CD163^+$ DC3 bulk RNAseq data displayed as a Radar plot showing the -Log(p-value) and the z-Score for each pathway using upregulated and downregulated DEG of each subset.

FIG. 13. (**A**) Manual gating strategy to define (as shown in FIG.14A) and sort cDC2 subsets used for bulk RNAseq analyses of FIG. 12F-H, starting from singlet, live $CD45^+$ cells. (**B**) The frequency among $CD45^+$ mononuclear cells of $CD163^+CD14^-$ and $CD163^+CD14^+$ DC3 subsets in the three patient groups defined in FIG. 12A-C is shown among $CD45^+$ PBMC. (**C**) Pearson correlation of the frequency of $CD163^+CD14^-$ and $CD163^+CD14^+$ DC3 versus the SLEDAI disease score in SLE patients. (**D**) Meaning plots of the relative expression of other soluble mediators as in FIG. 12D.

FIG. 14. Serum from patients with active SLE preferentially activates inflammatory $CD163^+CD14^+$ DC3. (**A**) cDC2 subsets from healthy blood donors (n=3) were FACS-sorted and cultured overnight with serum from healthy donors (n=12), or patients with inactive (n=12) or active (n=12) SLE and 55 soluble mediators were quantified in the culture supernatants. The cDC2 subset secretomes (concentration of each soluble factor) in the culture supernatants were analyzed with UMAP. (**B**-**D**) In the Secretome-UMAP, each dot corresponds to one culture supernatant. Supernatants from (**B**) the four cDC2 subsets or from (**C**) the different patient groups are shown on the Secretome-UMAP projection. (**D**) Relative expression of pro-inflammatory soluble mediators involved in SLE

immunopathology. (**E**) Heat map showing the difference in soluble mediators' concentration between supernatants of cultures with SLE patient serum compared to healthy serum. P values were determined by comparing absolute concentrations in supernatants of cultures with SLE patient serum compared to healthy serum using Kruskal Wallis (non-parametric one-way ANOVA) followed by Dunn's multiple comparisons test.

FIG. 15. Frequency and proportion of DC2 and DC3 in healthy and disease. (**A**) Frequency among myeloid cells of DC2 and DC3 in the non-lesional and lesional skin of Atopic dermatitis or Psoriasis patients. (**B**) Frequency among total cDC2 (DC2+DC3) of DC2 and DC3 in the normal adjacent liver of within different tumour sectors from four Liver Hepatocellular carcinoma (HCC) patients. (**C-E**) PBMCs were isolated from healthy subjects (n=10), and patients with SLE (n=10) or systemic sclerosis (SSC; n=15), and cDC2 subsets were defined by FACS. (**C-D**) The frequency of cDC2 subsets in the three patient groups is shown among (**C**) $CD45^+$ PBMCs and (**D**) total cDC2s. P values were calculated using the Mann-Whitney test. (**E**) Pearson correlation of the frequency of $CD163^+$ ($CD14^-$ and $CD14^+$) DC3s versus the SLE disease activity score (SLEDAI) in SLE patients.

EXAMPLES

Example embodiments of the disclosure will be better understood and readily apparent to one of ordinary skill in the art from the following discussions and if applicable, in conjunction with the figures. It should be appreciated that other modifications related to structural, electrical and optical changes may be made without deviating from the scope of the invention. Example embodiments are not necessarily mutually exclusive as some may be combined with one or more embodiments to form new exemplary embodiments.

Results

Unbiased identification of new monocyte and DC specific markers using the InfinityFlow pipeline

To identify new monocyte-specific and DC-specific markers, 332 flow cytometry (FACS) stainings from a single human blood donor was carried out; all stainings included a set of 14 'backbone" markers (to define all known monocyte and DC subsets) and one "variable" PE-conjugated antibody (see Star Methods). It was reasoned that this experimental setting was amenable to machine learning approaches, to predict the signal from PE-conjugated antibodies (each measured on 1 staining out of 332) for all cells by a regression-based approach integrating the expression of backbone markers (measured in the 332 FACS stainings). To achieve this, Support Vector Machines (SVM) were used — a multi-purpose machine learning framework that is accurate, robust to noise and can be used for regression purposes and single-cell classification problems.

Using SVM regression and starting from live $CD45^{+}CD3^{-}CD20^{-}HLA\text{-}DR^{+}$ cells, 332 new flow cytometry files (fcs) that included the 14 backbone markers, the PE variable marker and 332 predicted variable markers were generated (FIG. 1A, Table S1). These generated files were processed using non-linear dimensionality reduction via t-stochastic neighbour embedding (tSNE) (Van der Maaten and Hinton, 2008) and Phenograph clustering (DiGiuseppe et al., 2018; Levine et al., 2015) algorithms using the 332 predicted dimensions (FIG. 1B and FIG. 2A-B). All previously described monocyte and DC subsets were delineated based on Phenograph clusters (n=24) and on known markers contained in the backbone staining but were shown to express new markers, including: CD45RO, CD93, HLA-A2, CD262 (TRAIL-R2/DR5), CD164, CD226 (DNAM-1), CD298, CD51 (Integrin αV), Integrin β5, CD81, CD275 (ICOS-L), CD54 (ICAM-1), FCRL6, CD290 (TLR10), Tim-3 (CD366), CD200 and CD319 (CRACC) for cDC1; Integrin β7, CD200R, CD180 and CD101 for cDC2; CD71, CD324 (Cadherin-1), CD271 (NGFR) and CD182 (CXCR2) for pre-DC; CD55, Mac-2, CD261 (TRAIL-R1), CD114 (CSF3R), CD35 (CR1), CD11b-activated and CD89 (FcαR) for classical monocytes (cMo); CD215 (IL-15RA) and CD105 for intermediate

monocytes (iMo); and CD102 (ICAM-2), CD52, CD282 (TLR2), CD88 (C5AR), CD85d, C3AR and CCR10 for non-classical monocytes (ncMo) (FIG. 1C, FIG. 2C and FIG. 3A).

The presence of pre-DC and their corresponding committed pre-cDC1 and pre-cDC2 fractions was recently described. While pre-cDC1 were too rare to be analyzed here, pre-cDC2, which are an intermediate between early pre-DC and cDC2, expressed CD22, CD26, CD181 (CXCR1), CD182 (CXCR2), CD183 (CXCR3), CD270 (HVEM), CD271, CD85g, CD294, CD324 (E-Cadherin), CD229, CD303, BTLA and CD319. Interestingly, pre-cDC2 had the highest HLA-DQ and Integrin β7 expression compared to all DC (FIG. 3B).

cDC2 include CD1c^{lo}CD14^{+} cells and are phenotypically different from monocytes

The analysis identified a need to clarify the relationship between cDC2 subsets and monocytes, as illustrated by the phenotypic overlap between cDC2 and cMo observed in the tSNE generated using the 332 predicted dimensions (FIG. 1B). When including the 332 predicted-dimensions, cDC2 and cMo were connected at their junction by cells that expressed low CD1c but intermediate-to-high CD14 expression (FIG. 1B and FIG. 2B). It was next addressed whether including only MNP discriminating markers defined in FIG. 1C could help resolve these subsets (FIG. 1D and FIG. 2D). Indeed, when reducing the analysis to only 92 MNP discriminating markers in a new tSNE space, the CD1c^{lo}CD14^{hi} cells were distant from monocytes and formed, together with cDC2, an independent population (FIG. 1D and FIG. 4A).

To identify the best markers to discriminate between cDC2 and cMo, Area Under the ROC Curve (AUC) statistics, which measures the overall specificity and sensitivity of a continuous variable to predict a binary one, was computed (FIG. 4A-B and FIG. 5A). While the commonly used cDC2 and cMo markers (CD1c and CD14 respectively) showed variable expression among cDC2, AUC analysis revealed several more resolutive markers, including FcεRIα and HLA-DQ as the best markers expressed by all cDC2, and CD88 and CD89 restricted to cMo (FIG. 4C and FIG. 5B-D).

A recent study addressed the heterogeneity of human blood monocytes and subsetised them into 8 clusters among which, cluster #8 comprised $CD14^+CD163^+CD1c^+$ cells that bound IgE, most probably through the IgE-Fc receptor ($Fc\varepsilon RI\alpha$). Interestingly, when applying a similar gating strategy (the "slan" marker being absent from the analysis, the inventors gated on $CD16^+CD14^{lo}$ monocytes to approximate $Slan^+$ monocytes, FIG. 5E), the InfinityFlow pipeline revealed that the cluster #8 cells in the study corresponded to $CD14^+$ cDC2 (FIG. 5F).

To confirm that $CD1c^{lo}CD14^{hi}$ cells were phenotypically related to cDC2 and not to cMo using real and not predicted protein expression, a Principal Component analysis (PCA) of the cells that fell in between cDC2 and cMo using the 14 backbone markers was carried out (FIG. 5G-J). The PC1 dimension, which explained the progression from cDC2 to cMo, was divided into 40 bins each containing 2.5% of the cells. These 40 bins were then processed by tSNE/Phenograph using their mean fluorescence intensity of the 332 predicted dimensions. The data confirmed that bins containing $CD1c^{lo}CD14^{hi}$ cells (Phenograph cluster #2) were connected to cDC2 bins (Phenograph #1) and distant from cMo bins (Phenograph #3) (FIG. 5I-J). Combining these discriminating markers by conventional FACS allowed clear delineation of $Fc\varepsilon RI\alpha^+CD1c^{+/lo}$ cDC2 from $CD88^+CD89^+CD14^+$ cMo, by both manual gating and the UMAP (Uniform Manifold Approximation and Projection for Dimension Reduction) dimensionality reduction algorithm (Becht et al., 2018; McInnes et al., 2018) (FIG. 4D-F and FIG. 5K). Note that by manual gating, some cells falling in the cDC2 population (UMAP space) were defined as cMo (black), confirming that unsupervised analysis outperforms classical manual gating (FIG. 4E-F).

To validate the findings in tissues other than blood, the inventors analyzed human blood, spleen and tonsil by Cytometry by Time-of-Flight (CyTOF). Using the discriminating markers mentioned above, it was found that cDC2 formed a clearly delineated population independent of monocytes/macrophages in these three tissues (FIG. 4G-H and FIG. 5L). Although all cells from each MNP subset (e.g. cDC2) from all tissues were regrouped in independent clusters in the tSNE space, they showed some phenotypic variation in-between tissues but the

discriminating marker expression patterns were conserved across tissues (FIG. 4I and FIG. 5M-O). The top cDC2 and cMo discriminating markers, FcεRIα/HLA-DQ and CD88/CD89 respectively, were expressed and remained discriminating in both the spleen and tonsil.

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CD1c^{lo}CD14^{+} cDC2 are FLT3L-dependent and clearly delineated from monocytes

A hallmark of cDC2 compared to monocytes is their dependency on FLT3 ligand (FLT3L) and transcription factors including IRF4 and KLF4 for 10 differentiation and proliferation. Analysis of seven patients that received FLT3L treatment (see Star Methods for patient information), showed that the proportions of both CD1c^{+}CD14^{-} and CD1c^{lo}CD14^{+} cDC2 (both being CD88$^{lo/-}$CD89$^{lo/-}$) were dramatically increased while the proportion of CD14^{hi}CD1c^{-} cMo was reduced (FIG. 4J-K and FIG. 5P) compared to before having received FLT3L (D0). In 15 addition, cMo exhibited low expression of the cDC2-specific IRF4 transcription factor that was highly expressed by CD1c^{+}CD14^{-} and CD1c^{lo}CD14^{+} cDC2 and the latter cells also expressed lower KLF4 and higher NOTCH2 than CD1c^{+}CD14^{-} cells (FIG. 4L). These findings are consistent with the functionally distinct murine cDC2 subsets defined in another study.

20 To further clarify the relationship between CD1c^{+}CD14^{+} cells, cDC2 and cMo at the gene expression level, the inventors index-sorted all blood cDC and monocytes from the Lin^{-}HLA-DR^{+} gate and analyzed the cells by single-cell RNA sequencing (scRNAseq) (FIG. 6A-B). The indexed (FACS) data from sorted cells was processed together with the FACS data of the full sample using tSNE 25 showing the distribution of sorted cells among DC subsets and monocytes (FIG. 7A and FIG. 6C). Here, 89% of sorted cells qualified for scRNAseq (SMARTseq2) and data analysis with the Seurat pipeline, and the Phenograph clustering algorithm identified eight cell clusters (FIG. 7B-C and FIG. 6D). Based on clusters' differentially expressed gene (DEG) and protein (indexed) expression, all 30 previously defined DC and monocyte subsets were identified, including cDC2 (clusters #2 and #4), monocytes (clusters #1 and #3, CD14^{hi}CD16^{-}; and cluster #7, CD16^{+} monocytes), and a population of contaminating cells expressing

natural killer (NK) cell signature genes (GZMH, NKG7 and GNLY) and at the protein level had a typical CD16$^{+/-}$HLA-DR^{lo} NK cell phenotype (cluster #5; FIG. 7C-D and FIG. 6F).

Next, it was addressed whether CD1c^{lo}CD14^{+} cells were related to cDC2 rather than to monocytes at the transcriptome level, as observed by the high dimensional protein expression analysis (FIG. 4A-I). Here, manual gating of DC subsets and monocytes was carried out using the indexed protein expression data. The inventors first confirmed the identity of the cell clusters obtained by the Seurat/Phenograph scRNAseq data analysis, and secondly demonstrated that CD1c^{lo}CD14^{+} cells were detected among cDC2 cluster #4 and were distinct from monocytes, thus confirming the protein-level findings at the RNA level (FIG. 7E-F, FIG. 6E and FIG. 6G).

Villani *et al.* recently proposed a new classification of human blood MNP, identifying six DC (DC1 to DC6), among which DC2 and DC3 were defined as two cDC2 subsets, and four monocyte (Mono1 to Mono4) subtypes by scRNAseq (Villani et al., 2017). It was found that the signature genes for DC1, DC2, DC5 (AXL^{+}SIGLEC6^{+} AS-DC) and DC6 identified by Villani *et al.* were enriched in cells defined here as cDC1, cDC2 (more in cluster #2 then #4), pre-DC and pDC, respectively. The highest expression of signature genes of DC3 (subset of cDC2) was detected in cMo cluster #1 and at also at a lower level in cDC2 #4. DC4 signature was the highest in CD16^{+} monocytes but not detected in any DC (FIG. 7G-H and FIG. 6H). The fact that Villani *et al.* defined the DC signature by comparing them to the other DC and not to monocytes could explain the high expression of monocyte-related genes by DC3, but the results indicate that DC4 could correspond to CD16^{+} monocytes. The inventors also compared how early pre-DC and DC5 (AS-DC) were defined by See *et al.* and Villani *et al.*, respectively (See et al., 2017; Villani et al., 2017) by conventional flow cytometry. AS-DC indeed comprised most pre-DC but also included CD45RA^{+}CD123^{lo}CD1c^{+} pre-cDC2 and AXL^{+}CD45RA^{-}CD1c^{+} cDC2 (FIG. 6J-K). The inventors next looked at the expression of signature membrane protein markers of DC1 to DC6, as defined at the RNA level by Villani *et al* (FIG. 7I). While DC1 (cDC1), DC2 (subset of cDC2), DC5 (AS-DC) and DC6 (pDC) markers

were highly expressed by cDC1 (CLEC9A, BTLA, CD135), cDC2 (CD1c, CD1d, FcεRIα), pre-DC (CD22, CD5, CD169) and pDC (CD85g, CD303, CD123), respectively, signature markers of DC3 (subset of cDC2; CD163, CD14, CD36) were expressed at a higher level by cMo and a subset of cDC2. The expression of DC4's ($CD1c^{-}CD141^{-}$ DC; CD16, CD85d, CD88) signature markers was restricted to monocytes and was the highest in $CD16^{+}CD14^{lo}$ ncMo, confirming the indexed-scRNAseq-based findings. Taken together, the RNA and protein data suggest that DC4 are $CD16^{+}$ monocytes while DC3 may be related to cMo.

However, Villani *et al.*, defined DC3 signature genes by comparing DC subsets with each other but not to monocytes, which could explain why their signature comprises mostly monocyte-related genes, such as S100A8, S100A9 and CD14. Because cDC2 clusters #2 and #4 were more enriched in DC2 and DC3 signature genes in the analysis, respectively (FIG. 7G-H and FIG. 6H), the inventors first performed a DEG analysis comparing clusters #2 and #4 and then a DEG analysis between cluster #4 and all other cells. In this way, new, specific cluster #4 (related to DC3) signature genes, including LMNA, CDKN1A and F13A1 (FIG. 6I) were revealed. As compared to cDC2 cluster #2, cDC2 from cluster #4, that correlate with Villani *et al.*'s DC3, expressed more monocyte-related genes, including CD14, S100A8 and S100A9 and were enriched for genes involved in the "role for IL-17A in Psoriasis" pathway. cDC2 from cluster #2, that correlate with Villani *et al.*'s DC2, expressed more genes of professional antigen presenting cells, including MHC-II molecules, and were enriched for genes involved in many DC-related pathways including the "antigen presentation" and the "Th1" and "Th2" pathways (FIG. 6L-M). It was also confirmed that the Mono1 and Mono3 signature genes identified by Villani *et al.* corresponded to cMo and that Mono2 corresponded to $CD16^{+}$ monocytes. Mono4 signature genes were detected only in cluster #5, which comprised contaminating NK cells (FIG. 7G-H).

<u>cDC2 are phenotypically, functionally and molecularly heterogeneous</u>

The study by Villani *et al.* unraveled cDC2 heterogeneity, and although they excluded $CD14^{+}$ cells in their gating strategy, it showed that this group of

cells could be sub-divided into two populations, DC2 and DC3. Since the inventors showed in the high dimensional protein (InfinityFlow) and scRNAseq analyses that CD1c^{lo}CD14^{+} cells are phenotypically related to cDC2 and not to monocytes, and comprised in the DC3-related subset of cDC2 (scRNAseq, cluster #4), the inventors aimed to address cDC2 heterogeneity in an unsupervised and unbiased manner. In the tSNE space obtained using the MNP discriminating markers from FIG. 1D, cDC2 was extracted and a PCA/Phenograph analysis using the 332 predicted markers (FIG. 8A-B and FIG. 9A) was performed. This analysis revealed that CD14, CD5 and CD163 were the top three loading markers that explained the greatest variance of the first two principal components (PC; FIG. 8C and FIG. 9B-C). CD5^{+} cells were all CD163^{-} CD14^{-} and showed the greatest expression of several markers also expressed by pre-DC and pre-cDC2 (FIG. 8D-E, FIG. 9D). Three populations among CD5^{-} cells were further identified: CD5^{-}CD163^{-} cells, CD163^{+}CD14^{-} cells and CD1c^{lo}CD163^{+}CD14^{+} cells, which had the greatest CD163 expression, as well as several monocyte-related markers, including CD11b and CD64. Non-linear dimensionality reduction (UMAP, isoMAP) and pseudo-time (NBOR, Wishbone) analyses confirmed the phenotypic progression from CD5^{+} cells, that expressed pre-DC-related markers, towards CD5^{-}CD163^{-} cells, then towards CD163^{+}CD14^{-} cells and finally CD163^{+}CD14^{+} cells (FIGs. S5E-G and S5H-K). Some of these pre-DC-related markers were also defined in a previous study at the RNA level (FIG. 9L). Note that Wishbone, a branching pseudo-time analysis method, revealed only one branch starting from CD5^{+} cells and finishing with CD163^{+}CD14^{+} cells, suggesting that the cells represent a differentiation and/or activation continuum. The four defined cDC2 subsets each had a set of markers that they specifically highly expressed (FIG. 8F). Interestingly, scanning electron microscopy analysis showed that CD5^{-}CD163^{+}CD14^{+} cells were the largest cells among cDC2 subsets and had a rougher and more granular membrane as compared to the others subsets and to CD88^{+}CD89^{+}CD14^{hi}CD16^{-} classical monocytes, both characteristics being often associated to a greater activation/maturation (FIG. 8G, FIG. 9M. These observations were confirmed by their greater size and granularity as determined by respective forward (FSC-A,

size) and side (SSC-A, granularity) scatter measured by flow cytometry (FIG. 8 H).

The FLT3L-dependency of these four cDC2 populations was also evaluated *in vivo* by profiling them in the blood of four FLT3L-injected patients (FIG. 10A and FIG. 11A). As compared to baseline (D0), cDC2 populations were all increased upon FLT3L injection (D14) as compared to $CD14^{hi}CD1c^{-}$ cMo, whose proportion was reduced.

Bulk RNAseq of the four cDC2 subsets was next carried out to evaluate their respective relationship with DC2 and DC3 (cDC2 subsets) described by Villani *et al.* (Villani et al., 2017). The phenotypic progression between cDC2 subsets (see FIG. 9H-K) was also observed at the RNA level: Connectivity map (cMAP) analysis of bulk RNAseq on the cDC2 subsets showed a strong enrichment of Villani's DC2 gene signature in $CD5^{+}$ cDC2 while the three other $CD5^{-}$ cDC2 subsets had a DC3 gene signature whose cMAP score progressed from $CD5^{-}CD163^{-}$ to $CD163^{+}CD14^{-}$ and was maximized in $CD163^{+}CD14^{+}$ cells (FIG. 10B). PCA followed by UMAP using the 10 first PCs analysis of these bulk RNAseq data showed that $CD5^{+}$ cells were regrouped while $CD5^{-}$ subsets were also regrouped but progressed from $CD5^{-}CD163^{-}$ to $CD163^{+}CD14^{-}$ cells and finally to $CD163^{+}CD14^{+}$ cells, confirming the DC2 versus DC3 signatures of $CD5^{+}$ cDC2 versus the three $CD5^{-}$ cDC2 subsets, respectively (FIG. 10C). Furthermore, in the scRNAseq analysis (FIG. 7B-H), all $CD5^{+}$ cDC2 were detected only in cDC2 cluster #2 that is related to Villani's DC2. The cMAP analysis and the observation of two clear clusters of cDC2 in the UMAP space confirmed the DC2/DC3 subsetization of cDC2: One cluster comprised only $CD5^{+}$ cells thus corresponding to DC2, while the three $CD5^{-}$ subsets formed a cluster corresponding to DC3. From now on, $CD5^{+}$ cells will be qualified as DC2, while $CD163^{-}CD5^{-}$, $CD5^{-}CD163^{+}CD14^{-}$ and $CD5^{-}CD163^{+}CD14^{+}$ cells will be qualified as DC3.

Note that these four subsets each had specific, highly expressed genes such as CD74 (MHC-II invariant gamma chain) and the pre-DC-related genes AXL, SIGLEC6 (CD327), CD5 and BLTA (as reported in (Villani et al., 2017)) for $CD5^{+}$ DC2, LTB (Lymphotoxin-β) for $CD5^{-}CD163^{-}$ DC3, CD109 for $CD163^{+}CD14^{-}$

DC3 and the monocyte-related genes S100A8, S100A9 and CD14 for $CD163^+CD14^+$ DC3 (FIG. 10D, FIG. 11B and Tables S3).

DC are the only cells able to activate and polarize naïve T cells. The inventors thus co-cultured allogeneic naïve $CD4^+$ T cells with DC2 and DC3 subsets to evaluate their potential functional specialization (FIG. 10E and FIG. 11C). While all subsets induced similar degrees of proliferation and Th1 polarization ($IFN\gamma^+$) of $CD4^+$ T cells, their capacity to induce $IL\text{-}4^+$ (Th2) and $IL\text{-}17^+$ (Th17) $CD4^+$ T cells progressively increased from $CD163^-$ (both $CD5^+$ DC2 and $CD5^-CD163^-CD14^-$ DC3) to $CD163^+CD14^-$ DC3 and finally $CD163^+CD14^+$ DC3. This higher Th17 polarizing capacity of $CD163^+$ DC3 (which was the highest for $CD163^+CD14^+$ DC3) confirmed the pro-Th17 signature observed in cDC2 cluster #4 (DC3) that was enriched in the $CD14^+$ DC3 subset of cDC2 (FIG. 6M). Interestingly, a study previously identified pro-Th17 inflammatory DC (infIDC) in ascites from patients with breast cancer, which were described as being monocyte-derived based on their gene signature that strongly correlated with that of *in vitro* monocyte-derived DC. Given the strong Th17 polarizing capacity of $CD163^+CD14^+$ DC3, it was hypothesized that they could correspond to circulating infIDC genes but would be related to cDC2 rather than monocytes. Strikingly, the only cells that strongly expressed infIDC-specific genes were $CD14^+$ cDC2 (subset of DC3) (FIG. 10F and Table S2). Putative "inflammatory" blood $CD14^+$ cDC2 also had the highest expression of CD206, TLR2 and TLR4, which were described as being highly expressed in infIDC. (FIG. 11D).

The inventors next carried out a pathway analysis of the cDC2 subset bulk RNAseq data of FIG. 10B-D. cDC2 subsets were enriched for genes involved in different pathways, with $CD5^+$ DC2 pathways partially overlapping with cDC2 cluster #2 (related to DC2) from FIG. 7B-C. $CD163^+CD14^+$ inflammatory DC3 shared 12.3% of their specific DEG with those of the described infIDC, while the three other subsets had no or only minimal overlap with infIDC (FIG. 11E). $CD163^+CD14^+$ inflammatory DC3 were also enriched in genes involved in "dendritic cell maturation", "production of nitric and reactive oxygen species (NOS and ROS) in macrophages", "phagosome formation", "death receptor signaling", "inflammasome pathway", "autophagy" pathways, as well as "Systemic Lupus

Erythematosus (SLE) Signaling", indicating their putative role in this disease (FIG. 10G).

Altogether, the high dimensional, single cell protein and RNA data analyses revealed a previously underestimated heterogeneity of blood cDC2. The inventors delineated, in an unbiased manner, blood inflammatory $CD1c^{lo}CD14^{+}$ cells (circulating inflDC) that were not included in the DC3 subset described by Villani *et al.*, because $CD14^{+}$ cells were excluded from their analysis.

Highly activated $CD163^{+}$ DC3 accumulate in the blood of lupus patients

DC can either induce adaptive immune responses or maintain tolerance, and autoimmunity occurs when this balance is lost. Interestingly, one of the top pathways identified from the bulk RNAseq of the cDC2 subsets was the "SLE Signaling" pathway in inflammatory $CD14^{+}$ DC3. The inventors thus evaluated the involvement of the newly defined cDC2 subsets in the blood of patients with SLE as compared to healthy subjects and patients with Systemic Sclerosis (SSc), another systemic autoimmune disease (see Materials and Methods for patient information). While the proportion of $CD5^{+}$ DC2 was comparable across all subjects, among $CD5^{-}$ DC3, a significant increase in total $CD163^{+}$ DC3 (both the $CD14^{-}$ and $CD14^{+}$ subsets) was observed, mirrored by a decrease in $CD163^{-}$ DC3 only in SLE patients (FIG. 12A-C and FIG. 13A-B). Importantly, the proportion of circulating $CD163^{+}$ DC3 significantly correlated with the SLE Disease Activity Index (SLEDAI, disease score) in SLE patients (FIG. 12D and FIG. 13C). SLE patient $CD163^{+}$ DC3 also showed increased expression of CD163 (a scavenger receptor) and CD169 (a type I interferon (IFN-I)-inducible marker), which were the highest on $CD163^{+}CD14^{+}$ DC3 (FIG. 12E).

The inventors carried out bulk RNAseq only on circulating $CD5^{+}$ DC2 and $CD163^{+}$ DC3, which could be sorted from healthy subjects and SLE patients in sufficient numbers for analysis (FIG. 12F-H). When comparing healthy subjects and SLE patients, most of the genes upregulated in SLE $CD5^{+}$ DC2 were IFN-I stimulated genes (ISG), but the vast majority of DEG were reduced in SLE patients (FIG. 12F-G and Table S3). This finding was in stark contrast to $CD163^{+}$

DC3 that showed a vast majority of upregulated genes in SLE patients, including ISG, but also several pro-inflammatory molecules, including TNFRSF10A (CD261/TRAIL-R1), LILRB1 (CD85j/ILT2) and TNFRSF21 (CD358/Death Receptor 6).

The higher maturation and activation state of $CD163^+$ DC3 in SLE patients were confirmed by pathway analysis, which showed a strong activation (positive z-score) of the "Death Receptor Signaling" and "Dendritic Cell Maturation" pathways (FIG. 12H). This latter pathway was also significant but strongly inhibited (negative z-score) in $CD5^+$ DC2. Pathway analysis also confirmed that most significant pathways of SLE $CD5^+$ DC3 were inhibited (negative z-score), and that strong positive activation of "Interferon (IFN-I) signaling" occurred in both $CD5^+$ DC2 and $CD163^+$ DC3. The overall inhibition of $CD5^+$ DC2 paralleled by the strong activation of $CD163^+$ DC3 in SLE patients underscores that cDC2 cannot be analyzed as a whole but must be considered individually as subsets to understand their role in the physiopathology of any disease.

<u>$CD14^+$ DC3 become highly pro-inflammatory in a SLE environment</u>

It was next addressed whether the SLE phenotype of healthy cDC2 subsets could be recapitulated in an SLE environment. The inventors first evaluated whether cDC2 subsets from healthy blood donors could be specifically activated when cultured in the presence of serum from inactive or active SLE patients or serum from healthy subjects (FIG. 14A). Unsupervised analysis using UMAP revealed that the secretomes of $CD163^+CD14^-$ DC3 and inflammatory $CD163^+CD14^+$ DC3 formed two independent clusters while those of $CD5^+$ DC2 and $CD163^-CD14^-$ DC3 were mostly regrouped (FIG. 14B), confirming the functional specialization of these cDC2 subsets. For both $CD163^+$ DC3 subsets, the secretomes further regrouped based on disease status, with sub-clusters comprising only secretomes obtained by culturing with active and inactive SLE ($CD163^+CD14^-$ DC3) and only active SLE (inflammatory $CD163^+CD14^+$ DC3) serum (FIG. 14C). Compared to cultures with serum from healthy subjects, only the two $CD163^+$ DC3 subsets significantly increased their secretory capacity when cultured with active SLE serum, especially inflammatory $CD163^+CD14^+$

DC3, which secreted more pro-inflammatory mediators known to participate in SLE physiopathology, such as BAFF, IL-1α, GRO-α (CXCL1), MCP-3 (CCL7), MIG (CXCL9), SDF-1 (CXCL12), IL-8, VEGF-A and TWEAK (FIG. 14D-E and FIG. 13D). These data reaffirm that cDC2 should not be studied as a whole, because when exposed to a pathologic environment (e.g. serum from SLE patients), cDC2 subsets show striking functional differences in their responses: both $CD163^+$ DC3 subsets, and particularly inflammatory $CD163^+CD14^+$ DC3, each show a specific and strong pro-inflammatory response.

Increased DC3 detected in diseased samples

In the context of inflammatory skin disease, matched non-lesional and lesional (diseased) skin from Atopic dermatitis (AD) and Psoriasis (PSO) patients were analysed by flow cytometry revealing a significant increase of DC3 specifically in the lesional skin of PSO patients (FIG. 15A). Next, flow cytometry analysis of matched normal adjacent liver tissue and different tumour sectors from four Liver Hepatocellular carcinoma (HCC) cancer patients showed an increased proportion of $CD14^+$ inflammatory DC3 in the tumour of the four patients as compared to their matched normal adjacent liver (FIG. 15B). An increase of the frequency of DC3 in the blood in Systemic lupus erythematosus (SLE) patients was also observed as compared to healthy blood donors (FIG. 15C), an increase that did not occur in systemic sclerosis patients (SSc) patients, another systemic autoimmune disease.

Discussion

Using high dimensional, single-cell protein and RNA expression analyses of human blood MNPs, the inventors have precisely delineated all MNP subsets and identified new markers to unambiguously define cDC2 and monocyte populations. The inventors have also unraveled cDC2 heterogeneity, revealing an FLT3L-responsive $IRF4^+CD14^+$ cDC2 subset that accumulates in the blood of patients with SLE and exhibits pro-inflammatory functions.

Villani *et al.* previously identified four monocyte (Mono1 to Mono4) and six DC (DC1 to DC6) populations in human blood (Villani et al., 2017). Mono1 and

Mono3 corresponded to classical $CD14^+CD16^-$ monocytes (cMo), Mono2 to $CD16^+$ monocytes and Mono4 was proposed to constitute a previously undefined population. Back mapping this population onto the indexed-scRNAseq analysis revealed that Mono4 signature genes were exclusively expressed by a cluster of cells expressing GZMH, NKG7 and GNLY NK cell signature transcripts and thus the inventors identified them as $CD16^{+/-}$HLA-DR^{lo} NK cells. In agreement with the conclusion, Günther *et al.*, who have established an updated consensus map of the human blood MNP system using indexed-scRNAseq (Günther, 2019), also concluded that the Mono4 population corresponded to HLA-$DR^-CD16^+CD56^-$ NK-cells, which likely contaminated the monocyte populations identified by Villani *et al.*

Concerning DC subsets, DC1 and DC6 identified by Villani *et al.* corresponded to the previously described cDC1 and pDC subsets, respectively, while DC2 and DC3 corresponded to two cDC2 subsets; the later cells expressed CD163 and were qualified as inflammatory DC. However, Villani *et al.* also identified two other previously un-described DC subsets: DC4 ($CD141^-CD1c^-$) and a rare DC5 ($AXL^+SIGLEC6^+$/AS-DC) subset. The present data confirmed the identity of DC1 as cDC1, DC2 and DC3 as cDC2 and DC6 as pDC. Günther *et al.* also showed that pre-DC and DC5 overlapped in their map, but that DC5 represented a larger population that also overlapped with the DC2 subset of cDC2, as defined both by the gating strategies used by Villani *et al.* and See *et al.*. It was also confirmed that DC5 signature genes were most highly expressed by pre-DC, but that DC5 also included pre-cDC2 and some $AXL^+CD45RA^-$ DC2 (FIG. 6J-K), these later being also $CD5^+$ (data not shown). Concerning $CD141^-CD1c^-$ DC4, Villani *et al.* showed that these cells expressed CD14, C5AR (CD88, one of the top two monocyte markers) and FCGR3A (CD16). Günther *et al.* reclassified these cells as $CD16^+$ non-classical monocytes (ncMo), which is in line with the indexed-scRNAseq data showing enrichment of DC4 signature genes in $CD16^+$ monocytes. This finding is also in agreement with a recent report that proposed that DC4 rather correlated with a subset of $CD14^{dim/-}CD16^-$ monocytes. Altogether, the findings regarding DC4 and Mono4 are in line

with those of Günther *et al.*, who have demonstrated that these two cell types are $CD16^{+}slan^{+/-}CD14^{lo}$ ncMo and $CD56^{-}$ NK cells, respectively (Günther, 2019).

In the indexed-scRNAseq data, Villani *et al.*'s top DC2 and DC3 signature genes mapped with cDC2 cluster #2 and cluster #4, respectively, that respectively contained all $CD5^{+}$ cDC2 and most $CD14^{+}$ cDC2. Further, both the InfinityFlow protein expression and the bulk RNAseq analyses revealed that $CD5^{+}$ cDC2 and the three subsets of $CD5^{-}$ cDC2 showed the greatest expression of DC2 and DC3 protein and signature genes, respectively. Altogether, $CD5^{+}$ cDC2 correspond to DC2 and $CD5^{-}$ cDC2 (three subsets) correspond to subsets of DC3. Because Villani *et al.* stringently excluded $CD14^{+}$ cells to sort DC, they may have only captured a minor fraction of the inflammatory $CD14^{+}$ subset of DC3 defined here. Rather, the $CD163^{+}$ DC3 that Villani *et al.* qualified as "inflammatory" based on CD14 and S100A9 expression likely correspond to the minor $CD163^{+}CD14^{-}$ DC3 subset that the inventors defined. Here, in addition to extend the phenotypic characterization of this DC3 subset, the inventors functionally demonstrated the inflammatory nature of $CD14^{+}$ DC3, which are not only increased in number, but are also reprogrammed to enhance their pro-inflammatory function in the blood of patients with SLE. The inventors further demonstrated their pro-inflammatory potential because $CD14^{+}$ DC3 from healthy donors had a highly pro-inflammatory secretome triggered by the serum of patients with active SLE. Although $CD163^{+}CD14^{-}$ DC3 were also increased in the patient's blood, they secreted intermediate quantities of pro-inflammatory mediators, at a higher level than $CD5^{+}$ DC2 and $CD163^{-}CD14^{-}$ DC3 but at a lower level than inflammatory $CD14^{+}$ DC3. While $CD5^{+}$ cells were separated from the three other subsets in the UMAP analysis of the bulk RNAseq data, the three other $CD5^{-}$ cDC2 subsets (DC3) were connected both at the protein and RNA levels and progressed from $CD5^{-}CD163^{-}$ to $CD163^{+}CD14^{-}$ and finally towards $CD163^{+}CD14^{+}$ cells, as confirmed by NBOR and Wishbone pseudo-time analyses. This progressive conversion was also suggested by the observation of an inversely correlated proportion of $CD5^{-}CD163^{-}$ and $CD163^{+}CD14^{+/-}$ DC3 in the blood of patients with SLE. These results confirmed that $CD5^{+}$ DC2 may represent an independent population corresponding to Villani *et al.*'s DC2 that

differs from the $CD5^-$ cDC2 (DC3) fraction (which rather contain populations at different stages of maturation and/or activation states). Future studies should aim to understand the relationship between these two populations in terms of their ontogeny and define whether $CD5^+$ cDC2 (DC2), which are molecularly and phenotypically related to pre-DC, can differentiate into $CD5^-CD163^{+/-}$ DC3 and finally into inflammatory $CD163^+CD14^+$ DC3.

A study previously described a population of inflammatory DC (infIDC), described as monocyte-derived, in ascites from patients with breast tumors that strongly promoted Th17 $CD4^+$ T-cell polarization. Interestingly, infDC-specific genes mapped to $CD14^+$ cDC2, with the latter being also the greatest Th17 inducers. Furthermore, cDC2 cluster #4 (indexed-scRNAseq data), which contained most $CD14^+$ DC3, were enriched in genes involved in the "Role of IL-17A in Psoriasis" pathway, confirming that *in vivo*, $CD14^+$ DC3 are programmed to favor Th17 polarization. It was also observed that $CD14^+$ DC3 have higher NOTCH2 and lower KLF4 expression compared to all the other cDC2. Another study also observed some heterogeneity among murine cDC2, with subsets expressing the KFL4 or NOTCH2 transcription factors that favor Th2 or Th17 polarization, respectively. Finally, all cDC2 subsets were shown to be responsive to FLT3L treatment; therefore, it was proposed that human inflammatory $CD14^+$ DC3 are not monocyte-derived, but rather belong to the DC lineage and could correspond to mouse $NOTCH2^+$ cDC2. In contrast to the murine data, however, these cells also primed naïve $CD4^+$ T cells towards Th2; this $CD4^+$ T-cell polarization is a hallmark of SLE, which is a B-cell-driven disease. The pro-inflammatory nature of $CD14^+$ DC3 was also confirmed by their high expression of CD354 (TREM1) protein and enrichment in genes involved in the "TREM1 signaling pathway". Further studies should address the role of TREM1 in inflammatory $CD14^+$ DC3, as it amplifies inflammatory responses triggered by bacterial and fungal infections by stimulating the release of pro-inflammatory chemokines and cytokines, as well as increased surface expression of activation markers. Finally, inflammatory $CD14^+$ DC3 were also enriched in genes from the "TWEAK signaling pathway" and TWEAK is one of the multiple pro-inflammatory

mediators involved in SLE immunopathology, which these cells secreted when cultured in the presence of active SLE patients' serum.

STAR Methods

Key Resources Table

REAGENT or RESOURCE	SOURCE	IDENTIFIER
Antibodies		
CADM1 (clone 3E1) Purified	MBL	Cat# CM004-3
CD11b (clone M1/70) Biotin	BD Biosciences	Cat# 553309
CD11c (clone B-Ly6) BV650	BD Biosciences	Cat# 563404
CD123 (clone 7G3) BUV395	BD Biosciences	Cat# 564195
CD135 (clone 4G8) BV711	BD Biosciences	Cat# 563908
CD14 (clone M5E2) BUV737	BD Biosciences	Cat# 564444
CD14 (clone M5E2) BV650	BD Biosciences	Cat# 563419
CD14 (clone BM-16) AF700	Biolegend	Cat# 350124
CD141 (clone AD5-14H12) APC	Miltenyi	Cat# 130-090-907
CD16 (clone 3G8) APC/Cy7	BD Biosciences	Cat# 302018
CD16 (clone 3G8) BV650	Biolegend	Cat# 563692
CD163 (clone GHI/61) BV605	Biolegend	Cat# 333616
CD169 (clone 7-239) PE	BD Biosciences	Cat# 565248
CD19 (clone SJ25C1) BV650	BD Biosciences	Cat# 563226

CD1c (clone L161) PercP/Cy5.5	Biolegend	Cat# 331514
CD1c (clone L161) BV421	Biolegend	Cat# 331526
CD1c (clone L161) PE/Cy7	Biolegend	Cat# 331516
CD2 (clone RPA-2.10) BV421	BD Biosciences	Cat# 562639
CD20 (clone 2H7) BV650	BD Biosciences	Cat# 563780
CD206 (clone 19.2) PE/CF594	BD Biosciences	Cat# 564063
CD268 (clone 11C1) PE/Dazzle594	Biolegend	Cat# 316922
CD3 (clone SP34-2) BV650	BD Biosciences	Cat# 563916
CD301 (clone H037G3) PE	Biolegend	Cat# 354704
CD303 (clone AC144) Biotin	Miltenyi	Cat# 130-090-691
CD33 (clone WM53) PE/CF594	BD Biosciences	Cat# 562492
CD34 (clone 581) AF700	BD Biosciences	
CD45 (clone HI30) V500	BD Biosciences	Cat# 560777
CD45RA (clone 5H9) FITC	BD Biosciences	Cat# 556626
CD45RA (clone L48) PE/Cy7	BD Biosciences	Cat# 337167
CD5 (clone UCHT2) BV711	BD Biosciences	Cat# 563170
CD88 (clone S5/1) PE/Cy7	Biolegend	Cat# 344308
CD89 (clone A59) BV510	BD Biosciences	Cat# 744375
CD89 (clone A59) APC	Biolegend	Cat# 354106
FcεR1α (clone AER-37 (CRA-1)) PerCP	Biolegend	Cat# 334616
FcεR1α (clone AER-37 (CRA-1)) APC/Cy7	Biolegend	Cat# 334632

HLA-DR (clone L243) BV785	Biolegend	Cat# 307642
IKAROS (clone R32-1149) BV421	BD Biosciences	Cat# 564865
IRF4 (clone 3E4) PE	eBioscience	Cat# 12-9858-82
IRF8 (clone V3GYWCH) PercP/eFluor710	eBioscience	Cat# 46-9852
KLF4 (clone NA) APC	R&D Systems	Cat# IC3640A
LAMP5 (clone 124-40B) PE	Biolegend	Cat# 355804
NOTCH2 (clone 16F11) PE	eBioscience	Cat# 12-5786-80
PU.1 (clone 7C6B05) Alexa Fluor 647	Biolegend	Cat# 658003
RelB (clone EP613Y) Alexa Fluor 488	Abcam	Cat# ab199089
112Cd_CD14 (clone TUK4)	Invitrogen	Cat# MHCD1400
141Pr_Clec12A (clone 687317)	R&D Systems	Cat# MAB2946
142Nd_CD5 (clone UCHT2)	Biolegend	Cat# 300602
143Nd_CD2 (clone RPA-2.10)	Biolegend	Cat# 300202
145Nd_CD68 (clone KP1)	eBioscience	Cat# 14-0688-80
146Nd_CD19 (clone HIB19)	eBioscience	Cat# 14-0199-82
146Nd_CD20 (clone 2H7)	eBioscience	Cat# 14-0209-82
146Nd_CD3 (clone OKT3)	Biolegend	Cat# 317302
147Sm_CD86 (clone IT2.2)	BD Biosciences	Cat# 555663
148Nd_CD45RA (clone HI100)	Biolegend	Cat# 304102
149Sm_HLA-DR (clone L243)	Biolegend	Cat# 307602
150Nd_CD80 (clone L307.4)	BD Biosciences	Cat# 557223

151Eu_CD141 (clone 1A4)	BD Biosciences	Cat# 559780
152Sm_CD1c (clone L161)	Biolegend	Cat# 331502
153Eu_FcεR1α (clone AER-37)	eBioscience	Cat# 14-5899-82
154Sm_CD87 (clone VIM5)	Biolegend	Cat# 336902
155Gd_CD33 (clone WM53)	BD Biosciences	Cat# 555449
156Gd_CD22 (clone HIB22)	Biolegend	Cat# 302502
157Gd_CXCR3 (clone 1C6)	BD Biosciences	Cat# 557183
158Gd_CD82 (clone ASL-24)	Biolegend	Cat# 342102
159Tb_CD301 (clone H037G3)	Biolegend	Cat# 354702
160Gd_CD206 (clone 19.2)	BD Biosciences	Cat# 555953
161Dy_CD123 (clone 7G3)	BD Biosciences	Cat# 554527
162Dy_CD88 (clone S5/1)	Biolegend	Cat# 344302
163Dy_BTLA (clone MIH26)	Fluidigm	Cat# 3163009B
164Dy_CD89 (clone A59)	Biolegend	Cat# 354102
165Ho_CD71 (clone CY1G4)	Biolegend	Cat# 334102
166Er_CD85d (clone 42D1)	Biolegend	Cat# 338704
167Er_Integrin-B7 (clone FIB504)	Biolegend	Cat# 321202
168Er_CD26 (clone BA5b)	Biolegend	Cat# 302702
169Tm_CD163 (clone GHI)	Biolegend	Cat# 333602

170Er_CD35 (clone 594708)	R&D Systems	Cat# MAB5748
171Yb_CD166 (clone 3A6)	Biolegend	Cat# 343902
172Yb_HLA-DQ (clone Tü169)	Biolegend	Cat# 361502
173Yb_CD294 (clone BM16)	Biolegend	Cat# 350102
174Yb_CD354 (clone TREM-26)	Biolegend	Cat# 314902
175Lu_CD172b (clone B4B6)	Biolegend	Cat# 323902
176Yb_CD11b (clone ICRF44)	Biolegend	Cat# 301302
209Bi_CD16 (clone 3G8)	Biolegend	Cat# 302002
89Y_CD45 (clone HI30)	Fluidigm	Cat# 3089003B
Biological Samples		
Buffy coat for the LegendScreen/InfinityFlow analysis	SingHealth, Singapore	N/A
Buffy coat for functional experiments	SingHealth, Singapore	N/A
PBMC from whole blood for scRNAseq analysis	SingHealth, Singapore	N/A
FLT3L-treated patients' whole blood PBMC	Icahn School of Medicine at Mount Sinai, Hess Center for Science and Medicine, New York, USA	N/A
SLE patients' whole blood PBMC	Department of Rheumatology and Clinical Immunology, University Medical Center Utrecht, Utrecht, The Netherlands	N/A
Serum from SLE patients	Department of Rheumatology and Clinical Immunology, University Medical Center	N/A

	Utrecht, Utrecht, The Netherlands	
Critical Commercial Assays		
LEGENDScreen™ Human PE Kit	Biolegend	Cat# 700007
Deposited Data		
SMARTseq2 single cell transcriptome data of human peripheral blood DC and monocytes	This paper	GEO: GSE132566
Microarray data of Segura *et al.*	Segura et al., 2013, J Exp Med. https//doi: 10.1084/jem.20121103	GEO: GSE40484
Software and Algorithms		
DIVA	BD Biosciences	https://www.bdbiosciences.com/en-us
FlowJo v.10.5.3	Tree Star Inc.	https://www.flowjo.com
SeqGeq	FlowJo, LLC	https://www.flowjo.com/solutions/seqgeq
GraphPad Prism 6	Graphpad	https://www.graphpad.com/scientific-software/prism/
R 4.4	The R Foundation	https://www.r-project.org
tSNE	Van Der Maaten et al., 2008, Journal of Machine Learning Research. https://doi.org/10.1007/s10479-011-0841-3	https://github.com/jkrijthe/Rtsne
UMAP	McInnes et al., 2018, arXiv:1802.03426	https://github.com/lmcinnes/umap
SVM regression used in InfinityFlow	The R Foundation	https://cran.r-project.org/web/packages/e1071
Seurat V2	Butler et al., 2018, Nature Biotech.	https://doi.org/10.1038/nbt.4096 https://satijalab.org/seurat/

Phenograph	Levine et al., 2015, Cell. doi:10.1016/j.cell.2015.05.047	https://github.com/JinmiaoChenLab/Rphenograph
NBOR	J. Chen et al., 2016, Nat. Commun. 7, 11988 (2016). https://doi: 10.1038/ncomms11988	https://github.com/JinmiaoChenLab/Mpath
Wishbone	M. Setty et al., 2016, Nat Biotechnol. https://doi: 10.1038/nbt.3569	https://github.com/ManuSetty/wishbone
cMAP	Haniffa et al., 2012. Immunity. https://doi: 10.1016/j.immuni.2012.04.012	Customized code
Salmon	Patro et al.,2017, Nat Methods. doi: 10.1038/nmeth.4197	https://github.com/COMBINE-lab/salmon
txImport	Soneson et al., 2015, F1000Research. https://doi: 10.12688/f1000research.7563.2	https://bioconductor.org/packages/release/bioc/html/tximport.html
DESeq2	Love, et al., 2014, Genome Biology. https: doi:10.1186/s13059-014-0550-8	https://bioconductor.org/packages/release/bioc/html/DESeq2.html
Ingenuity Pathway Analysis	Qiagen	https://www.qiagenbioinformatics.com/products/ingenuity-pathway-analysis/

Blood and serum samples

Human samples were obtained in accordance with a favorable ethical opinion from Singapore SingHealth and National Health Care Group Research Ethics Committees and from. Collection of the samples from Utrecht was approved by the Medical Ethical Committee from the University Medical Centre Utrecht. FLT3L-treated patient samples were obtained in accordance with a clinical protocol which was approved by the Mount Sinai Institutional Review Board and in accordance with U.S. Law. Written informed consent was obtained from all

donors according to the procedures approved by the National University of Singapore Institutional Review Board and SingHealth Centralised Institutional Review Board. Peripheral blood mononuclear cells (PBMC) used for the LegendScreen experiment (FIG. 1) were obtained from apheresis residue and PBMC used for the single cell RNAseq (scRNAseq) experiment (FIG. 7) were obtained from whole blood (two different donors). For functional experiments, PBMC were isolated by Ficoll-Paque (GE Healthcare) density gradient centrifugation of apheresis residue samples obtained from volunteer donors through the Health Sciences Authorities (HSA, Singapore). PBMC were obtained from 15 patients with systemic sclerosis (SSc), from 10 patients with systemic lupus erythematosus (SLE) that fulfilled the 1997 ACR classification criteria for SLE and from 10 healthy subjects. Healthy SSc, SLE patients' and healthy subjects' PBMC were all from the university medical centre (Utrecht, Netherlands) (Table S4). PBMC from 7 patients with follicular lymphoma or small lymphocytic lymphoma before and 11 days after having received FLT3L treatment were obtained from Mount Sinai Medical School (New York, U.S.A.) (Table S5). Serum samples were obtained from 24 patients with inactive (n=12) and active (n=12) SLE patients, and from 12 healthy subjects (Table S6). Spleen tissue was obtained from patients with tumors in the pancreas who underwent distal pancreatomy (Singapore General Hospital, Singapore). Tonsil tissue was obtained from patients with adeno-tonsillar obstruction and who underwent adeno-tonsillectomy (KK Hospital, Singapore). Spleen and tonsil tissues were processed as previously described (Haniffa et al., 2012).

LegendScreen and the InfinityFlow pipeline

PBMCs (700 million) were isolated by Ficoll-Paque (GE Healthcare) density gradient centrifugation of apheresis residue samples obtained from one volunteer donor identified through the Health Sciences Authorities (HSA, Singapore). Cells were incubated with Live/Dead blue dye (Invitrogen) for 30 min at 4℃ in phosphate buffered saline (PBS) and then incubated in 5% heat-inactivated fetal calf serum (FCS) for 15 min at 4℃ (Sigma Aldrich). The following 14 anti-backbone markers antibodies were added to the cells and incubated for 30 min

at 4℃, and then washed: CD123-BUV395 (clone 7G3), HLA-DR-BV786 (clone L243), CD5-BV711 (clone UCHT2), CD3-BV650 (clone SP34-2), CD20-BV650 (clone 2H7), CD45-V500 (clone HI30), CD2-BV421 (clone RPA-2.10), CD45RA-FITC (clone 5H9), CD14-AlexaFluor700 (clone M5E2), all from BD Biosciences; CD163-BV605 (clone GHI/61), CD1c-PercP/Cy5.5 (clone L161), CD88-PE/Cy7 (clone S5/1), CD16-APC/Cy7 (clone 3G8), all from Biolegend; CD141-APC (clone AD5-14H12, Miltenyi biotec). The cells were then stained with 332 different PE-conjugated antibodies (Table S1) using the LegendScreen® Human PE kit (Biolegend) following the manufacturer's instructions.

The InfinityFlow pipeline involves regression analysis of the intensities of the PE-bound markers using the intensities of the backbone markers. In detail, the compensated cytometry data were transformed using a logicle transformation with parameters w=0.1, t=500000, m=4.5 and a=0, as defined in the flowCore R package. For each fcs file of the Legend Screen (Biolegend) experiment, half of the events were randomly selected to train an epsilon-regression Support Vector Machine (SVM) model using the e1071 R package with default parameters, resulting in 332 SVM regression models. For each model, the PE-bound marker intensity was used as the response variable and the intensities of the backbone markers were used as independent variables. For each event, each SVM regression model was applied on its associated vector of backbone marker intensities to predict the intensities of 332 PE-bound markers. For each of the 332 initial Legend Screen fcs files, these 332 regressed values were transformed back to a linear intensity scale, concatenated with the backbone and the PE-marker expression values and exported back as 332 new single .fcs files.

These predictions were used as the input for t-distributed Stochastic Neighbor Embedding (t-SNE) dimensionality reduction (using the Barnes-Hut implementation of t-SNE from the Rtsne R package) and Phenograph clustering from the Rphenograph R package. For the analysis of cDC2 and monocyte discriminating markers (FIG. 4A-B), monocytes or cDC2 were identified in the tSNE space generated using all MNP discriminating markers. For each PE-conjugated predicted intensity vector, the unsigned Area Under the ROC Curve (AUC) was computed to summarize its ability to delineate cDC2 and monocytes.

PCA and binning analysis of CD163$^+$ cDC2 and cMo

From the 332 fcs files generated using the PBMCs stained with 14 anti-backbone marker antibodies and the LegendScreen® Human PE kit, cells gated using the strategy shown in FIG. 5G were exported and a PCA was performed using the mean fluorescence intensity (MFI) of the 14 backbone markers. In the resulting PCA space, cells were separated into 40 bins (each comprising 2.5% of the total cells) defined along the PC1 axis. The 40 bins were analyzed by tSNE/Phenograph using the MFI of the 332 variable PE markers.

Algorithms for dimensionality reduction and pseudo-time analyses

For CyTOF (FIG. 4G-I), scRNAseq (FIG. 7C) and Luminex data (FIG. 14B-D) marker, PC expression values and soluble mediators concentrations (respectively) were transformed using the logicle transformation function (Parks et al., 2006). For flow cytometry data, marker expression values were transformed using the auto-logicle transformation function from the flowCore R package.

tSNE and Uniform Manifold Approximation and Projection (UMAP) were carried out using all markers or significant PCs (based on Seurat analysis). For tSNE, the Rtsne function in the Rtsne R package with default parameters was used for flow cytometry and CyTOF data, and using a perplexity equal to 10 for the scRNAseq analysis. UMAP version 2.4.0 was implemented in Python, but executed through the reticulate R package to interface R objects with Python. UMAP was run using 15 nearest neighbors (*nn*), a *min_dist* of 0.2 and euclidean distance (Becht et al., 2018; McInnes et al., 2018). Phenograph clustering (Levine et al., 2015) was performed using all markers or significant PCs (based on Seurat analysis) before dimension reduction, and with the number of nearest neighbours equal to 30 for flow cytometry and CyTOF analyses and equal to 15 for scRNAseq analysis.

Isometric feature mapping (isoMAP) (Tenenbaum et al., 2000) dimension reduction was performed using vegdist, spantree and isomap functions in the vegan R package (Chen et al., 2016). The vegdist function was run with

method="euclidean". The spantree function was run with default parameters. The isoMAP function was run with the ndim equal to the number of original dimensions of the input data, and k=5.

Wishbone analysis (Setty et al., 2016) was conducted using the top 40 loading markers from the PCA in FIG. 8B-C. Candidate cells (n=106) that had high CD5 expression were selected as the start of the pseudo-time analysis. Then, the median pseudo-time trajectory was calculated and used for further NBOR analysis (Schlitzer et al., 2015b). The trajectory was separated into four bins as the NBOR input. NBOR then refined the order of cells and clustered the genes into four clusters. The smoothed marker expression values in each gene cluster were generated to illustrate the trend of expression in the clusters.

The results obtained from the tSNE, UMAP, isoMAP, Wishbone pseudo-time dimension and Phenograph analyses were incorporated as additional parameters and converted to .fcs files, which were then loaded into FlowJo to generate heatmaps of marker expression on the reduced dimensions.

Human cell flow cytometry: Labeling, staining, analysis and cell sorting

All antibodies used for fluorescence-activated cell sorting (FACS) and flow cytometry were mouse anti-human monoclonal antibodies (mAbs), except for the chicken anti-human CADM1 IgY primary mAb. The mAbs used for flow cytometry are listed in Table S7 and all flow cytometry panels are listed in Table S8. Briefly, 5 x 10^6 cells/tube were washed and incubated with Live/Dead blue dye (Invitrogen) for 30 min at 4 ℃ in PBS and then incubated in 5% heat-inactivated FCS for 15 min at 4 ℃ (Sigma Aldrich). The appropriate antibodies diluted in PBS with 2% FCS and 2 mM EDTA were added to the cells and incubated for 30 min at 4 ℃, and then washed and detected with the secondary reagents. For intra-cytoplasmic or intra-nuclear labeling or staining, cells were fixed and permeabilized with BD Cytofix/Cytoperm (BD Biosciences) or with eBioscience FoxP3/Transcription Factor Staining Buffer Set (eBioscience/Affimetrix), respectively according to the manufacturer's instructions. Flow cytometry was performed on a BD FACSFortessa (BD Biosciences) and the data were analyzed using BD FACSDiva 6.0 (BD Biosciences) or FlowJo v.10.5.3 (Tree Star Inc.).

Mass cytometry staining, barcoding, acquisition and data analysis

For mass cytometry, pre-conjugated or purified antibodies were obtained from Invitrogen, Fluidigm (pre-conjugated antibodies), Biolegend, eBioscience, Becton Dickinson or R&D Systems as listed in Table S9. For some markers, fluorophore-conjugated or biotin- conjugated antibodies were used as primary antibodies, followed by secondary labeling with anti-fluorophore metal-conjugated antibodies (such as the anti-FITC clone FIT-22) or metal-conjugated streptavidin, produced as previously described (Becher et al., 2014). Briefly, 3 x 10^6 cells/well in a U-bottom 96 well plate (BD Falcon, Cat# 3077) were washed once with 200 µL FACS buffer (4% FBS, 2mM EDTA, 0.05% Azide in 1X PBS), then stained with 100 µL 200 µM cisplatin (Sigma-Aldrich, Cat# 479306-1G) for 5 min on ice to exclude dead cells. Cells were then washed with FACS buffer and once with PBS before fixing with 200 µL 2% paraformaldehyde (PFA; Electron Microscopy Sciences, Cat# 15710) in PBS overnight or longer. Following fixation, the cells were pelleted and resuspended in 200uL 1X permeabilization buffer (Biolegend, Cat# 421002) for 5 min at room temperature to enable intracellular labeling. Bromoacetamidobenzyl-EDTA (BABE)-linked metal barcodes were prepared by dissolving BABE (Dojindo, Cat# B437) in 100mM HEPES buffer (Gibco, Cat# 15630) to a final concentration of 2 mM. Isotopically-purified $PdCl_2$ (Trace Sciences Inc.) was then added to the 2 mM BABE solution to a final concentration of 0.5 mM. Similarly, DOTA-maleimide (DM)-linked metal barcodes were prepared by dissolving DM (Macrocyclics, Cat# B-272) in L buffer (MAXPAR, Cat# PN00008) to a final concentration of 1 mM. $RhCl_3$ (Sigma) and isotopically-purified $LnCl_3$ was then added to the DM solution at a final concentration of 0.5 mM. Six metal barcodes were used: BABE-Pd-102, BABE-Pd-104, BABE-Pd-106, BABE-Pd-108, BABE-Pd-110 and DM-Ln-113.

All BABE and DM-metal solution mixtures were immediately snap-frozen in liquid nitrogen and stored at -80°C. A unique dual combination of barcodes was chosen to stain each tissue sample. Barcode Pd-102 was used at a 1:4000 dilution, Pd-104 at a 1:2000, Pd-106 and Pd-108 at a 1:1000, and Pd-110 and Ln-113 at a 1:500. Cells were incubated with 100 µL barcode in PBS for 30 min

on ice, washed in permeabilization buffer and then incubated in FACS buffer for 10 min on ice. Cells were then pelleted and resuspended in 100 µL nucleic acid Ir-Intercalator (MAXPAR, Cat# 201192B) in 2% PFA/PBS (1:2000), at room temperature. After 20 min, cells were washed twice with FACS buffer and twice with water before being resuspended in water. In each set, the cells were pooled from all tissue types, counted, and diluted to $0.5x10^6$ cells/mL. EQ Four Element Calibration Beads (DVS Science, Fluidigm) were added at a 1% concentration prior to acquisition. Cell data were acquired and analyzed using a CyTOF Mass cytometer (Fluidigm).

The CyTOF data were exported in a conventional flow-cytometry file (.fcs) format and normalized using previously-described software (Finck et al., 2013). Events with zero values were randomly assigned a value between 0 and –1 using a custom R script employed in a previous version of the mass cytometry software (Newell et al., 2012). Cells for each barcode were deconvolved using the Boolean gating algorithm within FlowJo. The $CD45^+Lin$ $(CD3/CD19/CD20)^-HLA\text{-}DR^+$ population of PBMC were gated using FlowJo and exported as an .fcs file.

Generation of indexed-sorting and SMARTseq2 single cell transcriptome data

PBMCs from a blood donor were indexed-sorted using the Indexed-sorting panel (Table S8) on a BD FACSARIAIII (BD Biosciences) into 96 well plates containing 3 µL Lysis buffer (see below) using a 70 µm nozzle. Single-cell cDNA libraries were prepared using the SMARTSeq v2 protocol (Picelli et al., 2014) with the following modifications: (i) 1 mg/ml BSA Lysis buffer (Ambion® Thermo Fisher Scientific, Waltham, MA, USA); and (ii) 200 pg cDNA with 1/5 reaction of Illumina Nextera XT kit (Illumina, San Diego, CA, USA). The length distribution of the cDNA libraries was monitored using a DNA High Sensitivity Reagent Kit on the Perkin Elmer Labchip (Perkin Elmer, Waltham, MA, USA). All samples were subjected to an indexed paired-end sequencing run of 2x151 cycles on an Illumina HiSeq 4000 system (Illumina, San Diego, CA, USA), with 300 samples/lane. Data are available through GEO (GEO: GSE132566).

Pre-processing, quality assessment and control and analysis of SMARTseq2 single cell transcriptome data

Paired-end raw reads were aligned to the human reference genome (GRCh38 version 25 release; Gencode)using RSEM version 1.3.0. Transcript Per Million read (TPM) values were calculated using RSEM and used for downstream analysis. Quality control, selection of highly variable genes, PCA, and differential gene analysis was performed using the Seurat R package. tSNE and UMAP were used for dimensionality reduction and cell clusters were identified using the phenograph algorithm, as detailed above. The expression levels of key signature genes by known cell types was used to annotate the cell clusters accordingly. Lastly, signature genes of six DC subsets and four monocyte subsets were extracted from a previous study by Villani *et al.*, (Villani et al., 2017) and the expression of the top 20 signature genes was overlaid on the data in a heatmap format (FIG. 7G) or as the mean expression of all signature genes as meaning plots (FIG. 7H). From the microarray data of Segura *et al.*, (GEO, accession number GSE40484; see below for more details on the analysis) (Segura et al., 2013), a list of inflammatory DC (inflDC)-specific genes [defined as the intersection of differentially expressed genes (DEG) between inflDC and the four other cell types] was generated and their mean expression was overlaid as meaning plots or as a violin plot compiled in Prism 8 (GraphPad) (FIG. 10F). All scRNAseq dot plots and meaning plots displaying the gene expression levels or mean signature genes were generated using SecGec software (Flow Jo LLC).

Analysis of microarray data from Segura et al.

To reanalyze microarray data from Segura *et al.* (Segura et al., 2013), comparisons were made on the original submitter-supplied processed data tables using the GEOquery and limma R packages from theBioconductor project (Davis and Meltzer, 2007; Smyth, 2004, 2005). The GEOquery R package parses GEO data into R data structures that can be used by other R packages.

Generation and analysis of bulk RNAseq data

cDNA libraries were prepared from 100 cells using the SMARTSeq v2 protocol (Picelli et al., 2014) with the following modifications: (i) 1 mg/ml BSA Lysis buffer (Ambion® Thermo Fisher Scientific, Waltham, MA, USA); (ii) addition of 20 µM TSO; and (iii) 200 pg cDNA with 1/5 reaction of Illumina Nextera XT kit (Illumina, San Diego, CA, USA). The length distribution of the cDNA libraries was monitored using a DNA High Sensitivity Reagent Kit on the Perkin Elmer Labchip (Perkin Elmer, Waltham, MA, USA). All samples were subjected to an indexed paired-end sequencing run of 2x151 cycles on an Illumina HiSeq 4000 system (Illumina, San Diego, CA, USA), with 23-24 samples/lane. Paired-end reads obtained from RNA sequencing were mapped to human transcript sequences obtained from Gencode version 28 (Harrow et al., 2012) using Salmon (version 0.9.1) (Patro et al., 2017). Transcript abundances quantified by Salmon were summarized to gene-level counts and normalized gene-level abundances in transcript per million (TPM) units using the tximport R/Bioconductor package (version 1.2.0). Cell subset-specific DEG were identified as those that were significantly upregulated or downregulated compared to all other cell subsets. To identify these genes, DEG analysis was performed using DESeq2 between each cell subset of interest and each of the other cell subsets. The maximum p-value (nominal) of the t-test in all comparisons (p_{max}) was used to control the type-I error rate with a threshold of $p_{max}<0.05$. After filtering for genes that were significant by p-value, the upregulated (or downregulated) genes were selected as those for which the fold change in all comparisons was consistently greater (or less) than zero. DEG heatmaps were generated using Log_2 TPM values. Genes modulated in a cell subset due to SLE were identified by performing DEG analysis that compared samples derived from SLE patients and healthy controls, where p-values adjusted for multiple testing correction by the Benjamini Hochberg method were used to control for the type-I error rate. For pathway analyses, lists of genes identified as cell subset-specific or SLE modulated by the abovementioned methods, together with the respective fold change and p-values, were supplied to Ingenuity Pathway Analysis™ (IPA) software. IPA analysis reported the p-value of enrichment of pathways in the supplied gene lists based on the

proportions of genes in a pathway that were differentially expressed. Based on the direction of the fold change, IPA predicted the up-regulation or down-regulation of pathways as a Z-score, where positive and negative scores implied predicted up-regulation and down-regulation, respectively. Within the significant pathways reported by IPA, 48 pathways relevant to the immunological response were shortlisted and radar plots were used to summarize the p-values and Z-scores of these pathways in a gene list. cMAP analysis (Lamb et al., 2006) was performed using lists of DEGs between DC2 and DC3 (up and low genes) published by Villani *et al.* For each bulk RNAseq sample, cMAP generated enrichment scores that quantified the degree of enrichment (or "closeness") to the given gene signatures. The enrichment scores were scaled and assigned positive or negative values to indicate enrichment for DC3 or DC2 signature genes, respectively.

Scanning Electron Microscopy

Scanning electron microscopy was performed as previously described (See et al., 2017).

Luminex® Drop Array™ assay on sorted cDC2 populations cultured in SLE patients' and healthy donors' serum

$CD5^+CD163^-$, $CD5^-CD163^-$, $CD5^-CD163^+CD14^-$ and $CD5^-CD163^+CD14^+$ cDC2 were sorted using a BD FACS ARIAIII (BD Biosciences) using the sort panel for stimulations and Luminex (Table S8). The cells ($2x10^3$) were cultured for 18 h in V-bottomed 96-well culture-treated plates (total volume, 50 µL) in Roswell Park Memorial Institute 1640 Glutmax media (Life Technologies) supplemented with 10% FBS, 1% penicillin/streptomycin (complete media) and in the presence of 2% serum from healthy subjects or SLE patients with an inactive or an active disease. After the 18 h stimulation, supernatants were collected for Luminex® analysis using the ProcartaPlex, Human Customized 55-plex Panel (Thermo Fisher Scientific, # PPX-55) to measure the following targets: APRIL, BAFF, BLC, ENA-78, Eotaxin, Eotaxin-2, Eotaxin-3, FGF-2, Fractalkine, G-CSF, GM-CSF, Gro-α, HGF, IFN-α, IFN-γ, IL-10, IL-12p70, IL-13, IL-15, IL-18,

IL-1α, IL-1β, IL-2, IL-20, IL-23, IL-27, IL-2R, IL-3, IL-31, IL-6, IL-7, IL-8, IL-9, IP-10, I-TAC, LIF, MCP-1, MCP-2, MCP-3, MDC, MIF, MIG, MIP-1α, MIP-1β, MIP-3α, MMP-1, SCF, SDF-1α, TNF-α, TNF-β, TNF-RII, TRAIL, TSLP, TWEAK, VEGF-A. Harvested supernatants were analysed using DA-Cell™ (Curiox Biosystems) Luminex® bead-based multiplex assays, which simultaneously measure multiple specific protein targets in a single sample. Using DA-Cell™, samples or standards were incubated with fluorescent-coded magnetic beads, which had been pre-coated with respective capture antibodies. After an overnight incubation at 4°C, the plates were washed twice. Biotinylated detection antibodies were incubated with the complex for 30 min and then Streptavidin-PE was added and incubated for a further 30 min. The plates were washed twice, then the beads were re-suspended with sheath fluid before acquiring on a FLEXMAP® 3D platform (Luminex) using xPONENT® 4.0 (Luminex) acquisition software. Data analysis was performed using Bio-Plex Manager™ 6.1.1 (Bio-Rad). Standard curves were generated with a 5-parameter logistic (5-PL) algorithm, reporting values for both MFI and concentration data. Normalized concentrations of analytes were transformed using the logicle transformation function (Parks et al., 2006) and analyzed using UMAP, as described above.

Allogenic mixed lymphocyte reaction

Naïve $CD4^+$ T cells were isolated from PBMCs using a Naïve $CD4^+$ T-Cell Isolation Kit II (Miltenyi Biotec), according to the manufacturer's instructions, and labeled with 5 μM CellTrace™ Violet dye (ThermoFischer) for 20 min at 20 °C. A total of 5,000 cells from sorted cDC2 subsets were co-cultured with 50,000 CFSE-labeled allogenic naïve T cells for 6 days in Iscove's Modified Dulbecco's Medium (Life Technologies) supplemented with 10% KnockOut™ Serum Replacement (Life Technologies). On day 6, the T cells were stimulated with 10 μg/ml phorbol myristate acetate (InvivoGen) and 500 μg/ml ionomycin (Sigma Aldrich) for 1 h at 37 °C. Then, 10 μg/ml Brefeldin A solution was added for 4 h, after which the cells were labeled with membrane markers (described above) and for intracellular cytokines (described below). Cells were fixed and permeabilized with BD Cytofix/Cytoperm (BD Biosciences), according to the manufacturer's instructions

and stained with cytokine-specific antibodies. Flow cytometry was performed using a BD LSRII or a BD FACSFortessa (BD Biosciences) and the data were analyzed using BD FACSDiva 6.0 (BD Biosciences) or FlowJo v.10 (Tree Star Inc.).

Statistical analyses

Significance for pathways analyses (see FIG. 10G, FIG. 12H and FIG. 6M) was defined by the IPA software (Qiagen). Differences in MFI for cDC2 subsets and cMo in FIG. 8H were defined by parametric one-way ANOVA followed by Tukey's multiple comparisons test. Friedman test (Non-parametric repeated measures ANOVA) followed by Dunn's multiple comparisons test was used to compare the capacity of the four cDC2 subsets to induce proliferation and cytokine production by $CD4^+$ T cells in the MLR experiments of FIG. 10E. Kruskal Wallis (non-parametric one-way ANOVA) followed by Dunn's multiple comparisons test was used to compare the median of each analyte produced by each cDC2 subset in the SLE groups against the healthy control group (see FIG. 14E). The Mann-Whitney test was used to compare data derived from patients with SLE versus healthy subjects or patients with SSc. Correlation coefficients and p values were calculated as the Pearson's correlation coefficient (see. FIG. 12D and FIG. 13C).

Supplementary Tables

Table S1 LegendScreen markers

PLATE	Tube No	Specificity	PLATE	Tube No	Specificity	PLATE	Tube No	Specificity
1	1	Blank	2	1	Blank	3	1	Blank
1	2	CD1a	2	2	CD86	3	2	CD220
1	3	CD1b	2	3	CD87	3	3	CD221 (IGF-1R)
1	4	CD1c	2	4	CD88	3	4	CD226 (DNAM-1)
1	5	CD1d	2	5	CD89	3	5	CD229 (Ly-9)
1	6	CD2	2	6	CD90 (Thy1)	3	6	CD231 (TALLA)
1	7	CD3	2	7	CD93	3	7	CD235ab
1	8	CD4	2	8	CD94	3	8	CD243

1	9	CD5	2	9	CD95	3	9	CD244 (2B4)
1	10	CD6	2	10	CD96	3	10	CD245 (p220/240)
1	11	CD7	2	11	CD97	3	11	CD252 (OX40L)
1	12	CD8a	2	12	CD99	3	12	CD253 (Trail)
1	13	CD9	2	13	CD100	3	13	CD254
1	14	CD10	2	14	CD101 (BB27)	3	14	CD255 (TWEAK)
1	15	CD11a	2	15	CD102	3	15	CD257 (BAFF)
1	16	CD11b	2	16	CD103	3	16	CD258 (LIGHT)
1	17	CD11bactiv	2	17	CD104	3	17	CD261 (TRAIL-R1)
1	18	CD11c	2	18	CD105	3	18	CD262 (TRAIL-R2)
1	19	CD13	2	19	CD106	3	19	CD263 (TRAIL-R3)
1	20	CD14	2	20	CD107a (LAMP-1)	3	20	CD266
1	21	CD15	2	21	CD108	3	21	CD267 (TACI)
1	22	CD16	2	22	CD109	3	22	CD268 (BAFF-R)
1	23	CD18	2	23	CD111	3	23	CD270 (HVEM)
1	24	CD19	2	24	CD112	3	24	CD271
1	25	CD20	2	25	CD114	3	25	CD273 (PD-L2)
1	26	CD21	2	26	CD115	3	26	CD274 (PD-L1)
1	27	CD22	2	27	CD116	3	27	CD275
1	28	CD23	2	28	CD117 (c-kit)	3	28	CD276
1	29	CD24	2	29	CD119	3	29	CD277
1	30	CD25	2	30	CD122	3	30	CD278 (ICOS)
1	31	CD26	2	31	CD123	3	31	CD279 (PD-1)
1	32	CD27	2	32	CD124	3	32	CD282 (TLR2)
1	33	CD28	2	33	CD126 (IL-6Rα)	3	33	CD284 (TLR4)
1	34	CD29	2	34	CD127 (IL-7Rα)	3	34	CD286 (TLR6)
1	35	CD30	2	35	CD129 (IL-9 R)	3	35	CD290
1	36	CD31	2	36	CD131	3	36	CD294
1	37	CD32	2	37	CD132	3	37	CD298
1	38	CD33	2	38	CD134	3	38	CD300e (IREM-2)
1	39	CD34	2	39	CD135	3	39	CD300F
1	40	CD35	2	40	CD137 (4-1BB)	3	40	CD301
1	41	CD36	2	41	CD137L	3	41	CD303

1	42	CD38	2	42	CD138	3	42	CD304
1	43	CD39	2	43	CD140a	3	43	CD307
1	44	CD40	2	44	CD140b	3	44	CD307d (FcRL4)
1	45	CD41	2	45	CD141	3	45	CD314 (NKG2D)
1	46	CD42b	2	46	CD143	3	46	CD317
1	47	CD43	2	47	CD144	3	47	CD318 (CDCP1)
1	48	CD44	2	48	CD146	3	48	CD319 (CRACC)
1	49	CD45	2	49	CD148	3	49	CD324 (E-Cadherin)
1	50	CD45RA	2	50	CD150 (SLAM)	3	50	CD325
1	51	CD45RB	2	51	CD152	3	51	CD326 (Ep-CAM)
1	52	CD45RO	2	52	CD154	3	52	CD328 (Siglec-7)
1	53	CD46	2	53	CD155 (PVR)	3	53	CD334 (FGFR4)
1	54	CD47	2	54	CD156c (ADAM10)	3	54	CD335 (NKp46)
1	55	CD48	2	55	CD158a/h	3	55	CD336 (NKp44)
1	56	CD49a	2	56	CD158b	3	56	CD337 (NKp30)
1	57	CD49c	2	57	CD158d	3	57	CD338 (ABCG2)
1	58	CD49d	2	58	CD158e1	3	58	CD340 (HER-2)
1	59	CD49e	2	59	CD158f	3	59	CD344 (Frizzled-4)
1	60	CD49f	2	60	CD161	3	60	CD351
1	61	CD50	2	61	CD162	3	61	CD352 (NTB-A)
1	62	CD51	2	62	CD163	3	62	CD354 (TREM-1)
1	63	CD51/61	2	63	CD164	3	63	CD355 (CRTAM)
1	64	CD52	2	64	CD165	3	64	CD357 (GITR)
1	65	CD53	2	65	CD166	3	65	CD360 (IL-21R)
1	66	CD54	2	66	CD167a (DDR1)	3	66	β2- micro-globulin
1	67	CD55	2	67	CD169	3	67	BTLA
1	68	CD56 (NCAM)	2	68	CD170 (Siglec-5)	3	68	C3AR
1	69	CD57	2	69	CD172a (SIRPa)	3	69	C5L2
1	70	CD58	2	70	CD172b (SIRPb)	3	70	CCR10
1	71	CD59	2	71	CD172g (SIRPg)	3	71	CLEC12A
1	72	CD61	2	72	CD178 (Fas-L)	3	72	CLEC9A

1	73	CD62E	2	73	CD179a	3	73	CX3CR1
1	74	CD62L	2	74	CD179b	3	74	CXCR7
1	75	CD62P	2	75	CD180 (RP105)	3	75	δ-Opioid Receptor
1	76	CD63	2	76	CD181 (CXCR1)	3	76	DLL1
1	77	CD64	2	77	CD182 (CXCR2)	3	77	DLL4
1	78	CD66a/c/e	2	78	CD183	3	78	DR3 (TRAMP)
1	79	CD66b	2	79	CD184 (CXCR4)	3	79	EGFR
1	80	CD69	2	80	CD193 (CCR3)	3	80	erbB3/HER-3
1	81	CD70	2	81	CD195 (CCR5)	3	81	FcεRIα
1	82	CD71	2	82	CD196	3	82	FcRL6
1	83	CD73	2	83	CD197 (CCR7)	3	83	Galectin-9
1	84	CD74	2	84	CD200 (OX2)	3	84	GARP (LRRC32)
1	85	CD79b	2	85	CD200 R	3	85	HLA-A,B,C
1	86	CD80	2	86	CD201 (EPCR)	3	86	HLA-A2
1	87	CD81	2	87	CD202b (Tie2/Tek)	3	87	HLA-DQ
1	88	CD82	2	88	CD203c (E-NPP3)	3	88	HLA-DR
1	89	CD83	2	89	CD205 (DEC-205)	3	89	HLA-E
1	90	CD84	2	90	CD206 (MMR)	3	90	HLA-G
1	91	CD85a (ILT5)	2	91	CD207 (Langerin)	3	91	IFN-g R b chain
1	92	CD85d (ILT4)	2	92	CD209 (DC-SIGN)	3	92	Ig light chain k
1	93	CD85g (ILT7)	2	93	CD210 (IL- 10 R)	3	93	Ig light chain λ
1	94	CD85h (ILT1)	2	94	CD213a2	3	94	IgD
1	95	CD85j (ILT2)	2	95	CD215 (IL- 15Rα)	3	95	IgM
1	96	CD85k (ILT3)	2	96	CD218a (IL-18Rα)	3	96	IL-28RA

PLATE	Tube No	Specificity
4	1	Blank
4	2	Integrin α9β1
4	3	integrin β5
4	4	integrin β7
4	5	Jagged 2
4	6	LAP
4	7	LT-bR

4	8	Mac-2
4	9	MAIR-II
4	10	MICA/MICB
4	11	MSC (W3D5)
4	12	MSC (W5C5)
4	13	MSC (W7C6)
4	14	MSC and NPC
4	15	MSCA-1
4	16	NKp80
4	17	Notch 1
4	18	Notch 2
4	19	Notch 3
4	20	Notch 4
4	21	NPC (57D2)
4	22	Podoplanin
4	23	Pre-BCR
4	24	PSMA
4	25	Siglec-10
4	26	Siglec-8
4	27	Siglec-9
4	28	SSEA-1
4	29	SSEA-3
4	30	SSEA-4
4	31	SSEA-5
4	32	TCR g/d
4	33	TCR Vβ13.2
4	34	TCR Vβ23
4	35	TCR Vβ8
4	36	TCR Vβ9
4	37	TCR Vδ2
4	38	TCR Vg9
4	39	TCR Vα24- Jα18
4	40	TCR Vα7.2
4	41	TCR α/β
4	42	Tim-1
4	43	Tim-3
4	44	Tim-4
4	45	TLT-2
4	46	TRA-1-60-R
4	47	TRA-1-81
4	48	TSLPR (TSLP-R)

Table S2 InflDC differentially expressed genes (DEGs)

Intersection of inflDC DEGs vs BDCA1 or CD14 or CD16 or inflMacro		inflDC vs BDCA1 blood cDC2 upregulated DEGs							
HPGDS		SPP1	IL10	P2RY12	RASGEF1B	GBGT1	OAS2	MRAS	C16orf45
CFI		FN1	FPR3	CD9	CAMSAP2	FMNL3	PTPRO	FMN1	NAV1

HPGD	CCL2	SPRED1	GALM	ITGB5	HMOX1	MYO1C	SMCO4	MX2
ADAM19	LYVE1	EGR3	TMEM51	TIMD4	CD84	CD1E	FABP3	IKZF2
TRPC6	CLEC5A	TREM2	ITGAM	CR1	EHD1	FBP1	SLC31A2	MIR222
MRC1	MMP12	FCGR3A	IL7R	HSPB1	IFITM3	AK4	SH3RF3	SAMD9
CD72	FCGR1A	IFIT3	IFI44L	NRP2	KIFC3	DSE	SERPINA1	MMP14
CCR4	GPNMB	CXCL10	EGR1	PLA2G15	YWHAH	DDX60L	ABCC5	ECM1
AXL	FCGR1CP	ABCA6	DOCK4	TCN2	STARD4	MARCH2	LAMP1	C11orf24
PARM1	C3AR1	OLFML2B	PIM1	CD72	UPP1	ADAP2	FLOT1	PROCR
CD226	CTSL	RGL1	C15orf48	BCL2A1	SIPA1L2	AMPD3	DHCR7	MRC2
GAS6	FAM20A	C1QA	RAPH1	HSPA1A	CECR6	VNN1	HSD3B7	LAP3
CD1E	ENPP2	RSAD2	HPGD	NECTIN2	TNFSF10	HLX	CD2	GPC4
FCGR2B	CCL4	IER3	PPARG	HSPA1A	CD226	RNF122	DPYSL3	GBA
CD2	A2M	LAMP3	CFB	HSPA1A	MARCO	DHRS3	SH3PXD2B	MANF
GPX7	C3	TLR7	MITF	IFITM1	MX1	GAPT	SQLE	XAF1
BCL2	RNASE1	SLC39A8	LRP12	ENDOD1	MLXIPL	NEK6	ITGAE	HCST
	ANKRD22	MS4A4A	ADAM19	ADM	LDLRAD3	PPIL1	GPX7	GK3P
	PLTP	NRP1	IFI6	CD81	RIN2	CCR5	CYYR1	TMEM52B
	C1QB	RHOBTB3	DHCR24	SDC4	SLC37A2	TNS1	LILRB1	CSF1R
	HPGDS	SLC7A8	MSLN	FPR1	GPR84	ARNTL2	ST14	DOCK1
	C1QC	CCL22	ALOX5AP	IL4I1	FPR2	PDIA4	CTSB	PDLIM7
	MERTK	PTGER2	TRPC6	NCEH1	GAS6	SGMS2	ANKH	SBNO2
	CD14	CX3CR1	FMNL2	TGM2	BCAR3	TLR1	SAMD9L	EPAS1
	TNFRSF11A	FLT1	SLAMF8	CXCL11	EHD4	MYOF	TBL2	LINC01001
	CCL4L2	SIGLEC1	CHST15	CTNS	OAS3	FILIP1L	MARCKS	CHSY1
	CCR1	CCND1	DRAM1	CCR4	HIVEP3	ADORA2B	PSD3	JAK3
	SLCO2B1	USP18	SERPING1	AXL	SRD5A3	TNFAIP8L3	FCGR2A	MAN1A1
	EGR2	PALLD	PTPN13	ARHGAP18	SCD	PLA2G4C	TTC7B	SDF2L1
	OLR1	MGAT4A	GPR82	SLC46A1	IRAK2	SLC43A3	FAM114A1	HSPA5
	LHFPL2	SIGLEC16	IDH1	TLR2	GBP2	FCGR2B	PTAFR	PROS1

	CFI	CD80	MRC1	VMO1	APOC1	ZFP36 L1	GK	GK
	DSC2	ITGA9	IFIT2	MMP2	CD180	PARP9	CD68	PLOD2
	ETV5	SLC1A 3	SUCN R1	PARM1	OAS1	RAB39 A	NABP1	BCL2
	IFIT1	CYP27 A1	SOCS3	TNFAIP 3	PLXNA 1	STXBP 1	TMEM3 7	PLEKH H1
	VSIG4	PLEK2	ITGB8	CDCP1	ADAMT SL4	CMPK2	DOK5	SCO2
	GPR34	SLC16 A10	FLVCR 2	FAM20 C	IL21R	LY6E	RRAS	RBM47
	BHLHE 41	ENG	EMP1	ATF5	TREML 1	SNX7	FICD	DNAJC 12
	MSR1	EPS8	PLAU	DDX58	BMP2K	LPAR5	RND3	CCDC 167
	USP41	MIR22 1	LAIR1	PAPSS 2	GNG12	CDYL2	PVR	TBC1D 14

Table S3 Differentially expressed genes (DEGs) FIG. 12F-G

Column header	**Description**
tpm.X	Expression level in transcripts per million units in the X subset, geometric mean over replicates
lfc.Y	Log2 fold change of population X / population Y comparison
p.Y	p-value of population X / population Y comparison
lfc.MostConservative	Minimum fold change among the three comparisons (or maximum in case of negative values)
p.Most Conservative	Maximum p-value among the three comparisons

CD5+ DC2 DEGs

geneSymbol	tpm.CD5+	lfc.CD163-	p.CD163-	lfc.CD14-	p.CD14-	lfc.CD14+	p.CD14+	lfc.MostConservative	p.Most Conservative
SLAMF7	42.88	3.17	2.02E-07	3.36	6.42E-09	4.80	1.56E-09	3.17	2.02E-07
VCAN	25.51	-2.62	2.75E-10	-2.12	1.18E-06	-3.32	1.41E-08	-2.12	1.18E-06
S100A8	38.76	-4.27	1.91E-06	-3.21	2.64E-09	-5.92	1.01E-05	-3.21	1.01E-05
ELOVL5	88.83	1.45	1.60E-04	1.15	5.03E-05	2.00	9.11E-05	1.15	1.60E-04
CD74	19617.75	1.33	1.71E-04	1.17	7.45E-05	2.26	2.30E-06	1.17	1.71E-04
C1orf162	1141.42	0.77	4.41E-04	1.39	1.98E-04	2.05	2.05E-06	0.77	4.41E-04
S100A9	339.67	-2.99	4.61E-04	-2.52	1.26E-10	-4.54	7.82E-06	-2.52	4.61E-04
ARHGDIB	1611.88	0.81	5.93E-04	0.91	4.58E-04	1.43	2.19E-04	0.81	5.93E-04
AXL	41.59	5.62	7.98E-12	2.81	3.44E-06	3.99	6.64E-04	2.81	6.64E-04

CES1	7.68	-4.08	1.84E-04	-3.21	2.64E-07	-3.20	7.02E-04	-3.20	7.02E-04
RAC1	110.46	-1.19	4.71E-04	-0.88	8.84E-04	-1.14	3.54E-05	-0.88	8.84E-04
ARHGEF1	35.78	-1.91	8.09E-08	-1.09	9.28E-04	-1.67	3.52E-06	-1.09	9.28E-04
HK3	2.71	-3.84	5.56E-05	-2.28	1.04E-03	-4.57	1.24E-10	-2.28	1.04E-03
MIR1248	1.75	-5.53	1.45E-04	-4.21	1.09E-03	-6.59	2.11E-04	-4.21	1.09E-03
MYL12A	1665.81	0.95	3.19E-05	0.88	1.56E-03	1.37	3.09E-05	0.88	1.56E-03
ACTG1	1722.97	0.76	1.32E-03	0.91	1.60E-03	1.54	2.37E-06	0.76	1.60E-03
ARPC2	1138.44	0.93	5.23E-04	0.85	1.71E-03	1.34	2.12E-04	0.85	1.71E-03
ADRBK1	21.32	-1.28	1.82E-04	-1.24	1.93E-04	-1.95	1.81E-03	-1.24	1.81E-03
B2M	25625.60	0.70	2.77E-05	0.87	2.35E-03	0.84	2.05E-03	0.70	2.35E-03
PRCP	183.58	1.13	3.91E-05	0.91	2.09E-03	2.05	3.08E-03	0.91	3.08E-03
YWHAZ	313.40	0.64	4.76E-04	0.59	3.16E-03	1.21	1.01E-06	0.59	3.16E-03
BTLA	3.60	5.70	3.20E-03	5.28	1.20E-06	5.92	4.04E-04	5.28	3.20E-03
C14orf1	9.42	2.77	2.38E-03	2.40	8.60E-04	2.59	3.28E-03	2.40	3.28E-03
VAV3	32.27	1.89	3.32E-03	1.14	1.49E-03	2.16	2.19E-03	1.14	3.32E-03
SPNS1	24.32	-1.69	4.75E-06	-1.38	2.56E-04	-1.82	3.48E-03	-1.38	3.48E-03
H3F3B	1872.25	0.77	3.51E-03	0.97	1.13E-03	1.69	1.17E-03	0.77	3.51E-03
FCN1	102.82	-1.38	3.65E-03	-1.66	9.61E-06	-2.07	7.94E-04	-1.38	3.65E-03
RETN	3.10	-3.09	6.29E-04	-2.78	3.70E-03	-4.67	1.67E-05	-2.78	3.70E-03
SARAF	320.01	1.11	2.79E-04	1.06	3.71E-03	1.17	6.96E-05	1.06	3.71E-03
TMEM39A	21.79	3.82	3.74E-03	1.83	1.49E-03	2.93	1.64E-06	1.83	3.74E-03
CAT	151.59	0.88	3.96E-03	1.59	1.64E-04	1.70	1.09E-03	0.88	3.96E-03
SIGLEC6	2.25	7.19	4.59E-03	7.61	2.87E-05	8.37	6.29E-05	7.19	4.59E-03
GDI2	286.29	0.74	4.91E-03	0.83	1.19E-04	1.58	1.03E-04	0.74	4.91E-03
NET1	11.17	3.44	4.90E-03	1.65	5.26E-03	4.18	2.29E-03	1.65	5.26E-03
VAMP7	21.00	3.14	5.38E-03	2.34	1.00E-03	1.51	4.29E-03	1.51	5.38E-03
ADAM28	154.49	2.65	5.60E-03	1.10	3.58E-06	3.83	8.43E-04	1.10	5.60E-03
LAMP1	0.43	-2.91	5.73E-03	-2.60	1.94E-05	-4.51	1.05E-05	-2.60	5.73E-03
PLXND1	1.18	-4.29	5.74E-03	-4.01	3.42E-07	-5.33	2.44E-09	-4.01	5.74E-03

CD207	1.05	6.30	5.79E-03	6.28	1.43E-04	8.40	8.82E-05	6.28	5.79E-03
COX7CP1	0.03	4.99	6.01E-03	4.99	6.01E-03	4.99	6.01E-03	4.99	6.01E-03
NEUROD2	0.50	-1.59	1.02E-04	-0.97	3.50E-03	-1.79	6.09E-03	-0.97	6.09E-03
MAPK1IP1L	64.83	2.09	6.11E-03	1.04	1.03E-04	1.84	1.12E-03	1.04	6.11E-03
S100A12	4.43	-4.22	6.37E-03	-2.83	1.63E-05	-5.46	7.71E-04	-2.83	6.37E-03
PAK1	182.23	1.51	6.57E-03	1.51	1.02E-03	1.89	1.88E-04	1.51	6.57E-03
ITM2C	10.64	1.60	5.23E-05	1.15	6.85E-03	4.05	9.71E-08	1.15	6.85E-03
TXNL4B	8.93	7.16	7.15E-04	2.35	7.03E-03	4.38	1.48E-06	2.35	7.03E-03
ALDH18A1	0.92	3.06	8.93E-04	2.78	7.58E-03	4.83	1.46E-03	2.78	7.58E-03
STAB1	0.70	-5.61	8.06E-03	-4.87	6.34E-08	-7.37	2.12E-08	-4.87	8.06E-03
LPIN3	0.30	-1.27	4.91E-04	-1.00	8.21E-03	-1.84	3.51E-04	-1.00	8.21E-03
KLF2	5.80	-2.45	4.09E-03	-1.70	2.56E-05	-2.61	8.54E-03	-1.70	8.54E-03
POGLUT1	21.98	3.16	8.57E-03	1.10	9.51E-04	1.58	7.50E-03	1.10	8.57E-03
AFF3	38.72	0.92	5.32E-04	0.88	8.64E-03	3.05	7.11E-08	0.88	8.64E-03
SDC3	0.66	-1.02	8.63E-03	-1.03	4.88E-03	-1.21	8.76E-03	-1.02	8.76E-03
DHRS7	107.09	1.00	1.27E-04	1.24	9.16E-04	1.58	9.06E-03	1.00	9.06E-03
TUBA1B	989.80	1.27	9.24E-03	1.31	7.53E-05	2.66	1.47E-03	1.27	9.24E-03
MARCH7	32.28	2.14	9.68E-03	0.72	3.40E-03	1.74	8.26E-03	0.72	9.68E-03
PYGB	1.09	-3.59	9.70E-03	-1.97	6.76E-03	-3.34	5.86E-05	-1.97	9.70E-03
DPP7	30.33	-1.41	6.57E-03	-1.00	1.04E-02	-1.79	1.34E-06	-1.00	1.04E-02
CSDE1	141.60	1.67	4.46E-03	0.79	2.79E-03	1.44	1.07E-02	0.79	1.07E-02
ARPC5	344.81	0.96	7.70E-03	0.77	1.88E-03	0.65	1.10E-02	0.65	1.10E-02
C6orf62	113.44	1.16	2.19E-03	1.04	5.03E-03	1.43	1.15E-02	1.04	1.15E-02
CAP1	277.95	1.61	1.15E-02	0.68	2.67E-04	1.39	5.65E-04	0.68	1.15E-02
SLC35F2	4.84	3.14	5.28E-04	2.28	1.16E-02	6.56	1.41E-05	2.28	1.16E-02
PLSCR1	311.43	1.17	1.17E-02	1.22	4.28E-03	1.91	1.00E-02	1.17	1.17E-02
SCOC	14.76	5.45	2.86E-07	2.93	7.95E-04	2.21	1.20E-02	2.21	1.20E-02
CEBPB	0.98	-2.33	1.23E-02	-2.72	6.60E-08	-3.58	1.14E-03	-2.33	1.23E-02
HIST2H3D	1.86	10.86	2.13E-06	5.40	1.24E-02	8.42	5.66E-03	5.40	1.24E-02

RABL6	1.45	-2.33	2.56E-03	-2.01	3.26E-05	-2.66	1.25E-02	-2.01	1.25E-02
TMEM156	13.85	3.43	1.25E-02	1.28	3.38E-03	3.58	2.22E-04	1.28	1.25E-02
MYD88	137.83	2.35	1.26E-02	1.10	2.31E-03	2.04	1.32E-03	1.10	1.26E-02
SMG9	6.33	-1.87	1.28E-02	-1.32	1.02E-02	-2.01	4.10E-03	-1.32	1.28E-02
ACTB	8688.24	0.74	1.28E-02	0.71	2.55E-03	0.98	3.21E-05	0.71	1.28E-02
PSMB4	643.80	0.94	6.45E-03	0.92	4.35E-03	0.86	1.29E-02	0.86	1.29E-02
NPM1	545.66	1.18	1.31E-02	0.88	2.28E-03	1.21	2.24E-03	0.88	1.31E-02
UGCG	27.64	2.54	1.31E-02	1.45	7.39E-05	3.06	6.15E-03	1.45	1.31E-02
TNK2	4.49	-2.04	1.32E-02	-1.20	4.41E-03	-1.75	9.67E-03	-1.20	1.32E-02
HMGN1	184.86	0.93	1.25E-02	0.70	1.32E-02	1.57	7.96E-03	0.70	1.32E-02
C1orf228	0.37	-3.99	1.33E-02	-4.12	5.86E-04	-6.42	1.53E-04	-3.99	1.33E-02
CD5	13.61	4.64	1.36E-02	6.08	1.91E-10	7.92	1.65E-03	4.64	1.36E-02
MYO9B	32.94	-1.96	3.68E-03	-1.02	1.28E-03	-1.17	1.36E-02	-1.02	1.36E-02
CTPS1	35.38	3.29	1.37E-02	1.29	4.62E-04	2.77	3.46E-03	1.29	1.37E-02
TMEM131	19.52	3.85	8.56E-05	0.79	1.37E-02	1.81	2.46E-03	0.79	1.37E-02
PLEKHG3	0.04	-7.07	1.39E-02	-3.79	3.82E-03	-5.27	4.82E-03	-3.79	1.39E-02
CYB5B	30.97	2.84	8.42E-03	1.37	3.39E-03	2.26	1.40E-02	1.37	1.40E-02
MSL3	42.51	1.79	3.32E-03	0.82	1.41E-02	1.74	3.92E-04	0.82	1.41E-02
RPS28	406.47	-1.05	1.34E-02	-0.71	1.42E-02	-1.74	1.25E-03	-0.71	1.42E-02
RPLP2	504.43	-1.11	3.48E-04	-0.57	1.44E-02	-1.30	3.55E-03	-0.57	1.44E-02
ZFR	45.72	0.87	2.42E-03	0.83	1.47E-02	1.61	4.83E-03	0.83	1.47E-02
IFNL1	0.29	6.15	1.50E-02	4.62	1.82E-03	8.17	1.15E-06	4.62	1.50E-02
CDK5RAP3	71.71	-1.34	1.03E-02	-0.76	1.51E-02	-1.41	8.48E-05	-0.76	1.51E-02
FARS2	17.25	2.93	1.52E-02	2.29	1.14E-02	4.39	2.54E-03	2.29	1.52E-02
DDX5	828.62	0.85	1.63E-02	0.97	3.39E-03	1.31	2.86E-05	0.85	1.63E-02
RAC2	216.74	1.04	1.64E-02	0.95	4.08E-03	1.08	2.76E-03	0.95	1.64E-02
OR9K1P	0.03	-3.09	1.66E-02	-2.65	3.22E-03	-3.58	6.89E-04	-2.65	1.66E-02
RBBP4	62.11	2.09	1.74E-02	1.15	2.27E-03	3.00	1.90E-04	1.15	1.74E-02
HSPA8	438.79	0.86	1.78E-02	0.98	4.25E-03	1.01	8.32E-04	0.86	1.78E-02

TINCR	0.05	-5.09	1.79E-02	-2.96	9.20E-03	-6.35	9.18E-03	-2.96	1.79E-02
BEND5	1.26	7.82	1.52E-02	4.71	9.88E-03	6.46	1.81E-02	4.71	1.81E-02
EIF2S3	152.86	0.51	1.81E-02	0.54	4.35E-03	1.22	2.42E-04	0.51	1.81E-02
GTF2IP18	0.06	-3.86	7.26E-03	-2.00	6.37E-03	-3.88	1.83E-02	-2.00	1.83E-02
ARHGAP5	28.62	1.69	1.84E-02	1.20	4.67E-03	3.11	1.08E-03	1.20	1.84E-02
EIF3E	363.38	0.44	4.33E-03	0.38	1.85E-02	0.94	5.56E-03	0.38	1.85E-02
CXCR4	547.33	1.23	1.46E-02	1.04	1.89E-02	2.04	3.14E-06	1.04	1.89E-02
CD48	477.56	1.09	5.95E-03	1.12	1.19E-03	1.09	1.90E-02	1.09	1.90E-02
RPL37A	675.50	-0.68	1.91E-02	-0.49	1.34E-02	-1.07	5.63E-03	-0.49	1.91E-02
TMEM14C	152.18	1.24	8.82E-03	0.80	1.91E-02	1.68	5.76E-03	0.80	1.91E-02
VCL	33.65	0.90	1.91E-02	1.06	1.80E-03	1.58	7.99E-04	0.90	1.91E-02
BRK1	295.26	1.23	1.91E-02	0.82	1.26E-02	1.49	7.27E-03	0.82	1.91E-02
HCST	68.16	-1.82	1.92E-02	-1.33	9.35E-06	-2.58	1.42E-04	-1.33	1.92E-02
FEM1C	4.92	2.75	5.08E-06	1.41	9.07E-03	0.99	1.94E-02	0.99	1.94E-02
RHOC	144.57	2.03	6.05E-03	0.95	1.40E-03	1.07	1.96E-02	0.95	1.96E-02
MYL12B	503.83	1.05	1.31E-05	0.86	1.97E-02	0.77	6.13E-03	0.77	1.97E-02
ANKRD44	117.23	1.96	3.39E-04	0.81	1.31E-02	0.93	2.01E-02	0.81	2.01E-02
PDIA3	154.05	1.14	2.02E-02	0.67	1.74E-02	1.19	4.25E-04	0.67	2.02E-02
S100A6	636.40	-0.79	3.02E-03	-0.51	2.05E-02	-1.44	3.04E-04	-0.51	2.05E-02
F13A1	1.03	-5.43	2.05E-02	-4.60	1.58E-05	-4.60	2.88E-03	-4.60	2.05E-02
ZRSR1	0.03	4.75	2.11E-03	3.67	2.11E-02	4.75	2.11E-03	3.67	2.11E-02
MOB1A	87.13	0.79	2.12E-02	1.06	6.04E-04	1.29	2.49E-03	0.79	2.12E-02
GLTSCR2	22.00	-0.98	4.34E-03	-0.70	2.12E-02	-1.45	6.59E-03	-0.70	2.12E-02
BASP1	35.11	1.38	2.22E-02	0.89	5.06E-04	2.25	1.34E-03	0.89	2.22E-02
MET	0.01	-2.77	1.40E-02	-2.89	8.41E-03	-3.42	2.24E-02	-2.77	2.24E-02
NIPA2	38.90	2.59	9.75E-04	1.18	9.22E-03	2.22	2.26E-02	1.18	2.26E-02
RRM1	12.66	2.12	2.26E-02	1.56	1.43E-02	2.26	2.53E-03	1.56	2.26E-02
MAPK1	18.55	2.85	1.76E-02	1.17	6.06E-04	1.35	2.28E-02	1.17	2.28E-02
TSPYL1	24.93	2.60	2.29E-02	1.04	8.67E-03	0.73	7.41E-03	0.73	2.29E-02

FGF23	2.52	-1.14	3.71E-03	-0.71	1.33E-02	-1.25	2.30E-02	-0.71	2.30E-02
VN1R81P	0.01	3.33	2.31E-02	3.33	2.31E-02	3.33	2.31E-02	3.33	2.31E-02
CD163	18.36	-2.08	2.32E-02	-2.25	1.95E-06	-2.45	2.38E-03	-2.08	2.32E-02
H2AFZ	411.34	0.44	2.30E-02	0.81	9.43E-04	1.37	2.32E-02	0.44	2.32E-02
EGR1	7.98	-1.95	2.33E-02	-1.89	1.57E-04	-2.21	6.47E-04	-1.89	2.33E-02
FAM129B	0.13	-7.13	2.33E-02	-3.76	1.18E-04	-5.64	1.91E-03	-3.76	2.33E-02
CD63	161.76	-0.71	1.73E-02	-0.48	2.34E-02	-1.27	2.87E-08	-0.48	2.34E-02
RQCD1	48.77	2.70	2.36E-02	0.82	5.65E-03	1.13	6.27E-03	0.82	2.36E-02
ANXA5	494.05	0.69	2.38E-02	0.79	1.26E-02	1.35	2.31E-04	0.69	2.38E-02
LY75	13.86	1.57	8.20E-04	1.18	2.97E-03	2.26	2.39E-02	1.18	2.39E-02
PPT1	260.19	1.34	2.43E-02	0.99	1.65E-02	1.23	7.15E-04	0.99	2.43E-02
AP1S2	313.63	1.17	2.46E-02	1.13	8.13E-04	0.95	1.01E-04	0.95	2.46E-02
MZT2B	10.71	-2.66	1.40E-04	-0.76	2.47E-02	-1.76	1.54E-03	-0.76	2.47E-02
HEPACAM	0.20	-1.47	7.59E-05	-0.71	1.49E-02	-1.48	2.47E-02	-0.71	2.47E-02
NMD3	25.52	1.90	7.80E-03	1.06	2.43E-02	2.21	2.48E-02	1.06	2.48E-02
TPP1	117.50	0.75	2.52E-02	0.58	1.04E-02	1.18	2.19E-03	0.58	2.52E-02
RAP2B	25.51	1.30	2.39E-02	0.65	2.54E-02	1.05	1.00E-02	0.65	2.54E-02
KBTBD4	0.11	6.83	1.51E-04	3.75	2.55E-02	4.32	1.15E-02	3.75	2.55E-02
FAM50A	7.40	-1.71	1.74E-02	-1.19	2.58E-02	-2.35	1.12E-02	-1.19	2.58E-02
SHKBP1	65.03	-1.92	1.53E-02	-0.75	2.61E-02	-1.26	9.61E-03	-0.75	2.61E-02
NOG	0.53	-1.00	4.33E-03	-0.72	2.65E-02	-1.57	1.11E-04	-0.72	2.65E-02
HNRNPA1L2	1.16	6.42	1.68E-02	2.36	2.66E-02	2.99	1.20E-03	2.36	2.66E-02
FLT3	50.03	1.86	2.71E-02	0.97	1.59E-02	2.33	3.45E-04	0.97	2.71E-02
CIDECP	28.22	4.21	3.27E-03	1.12	2.72E-02	3.01	2.06E-02	1.12	2.72E-02
PEF1	43.45	3.12	2.08E-03	1.68	2.72E-02	1.31	1.46E-02	1.31	2.72E-02
GLRX3	90.02	1.18	6.58E-03	0.54	1.70E-02	0.86	2.73E-02	0.54	2.73E-02
CLEC4A	339.84	0.43	2.76E-02	0.91	1.61E-04	2.47	1.69E-03	0.43	2.76E-02
CCDC66	16.12	2.83	4.58E-03	1.25	2.76E-02	1.24	6.25E-03	1.24	2.76E-02
ZNF410	27.74	3.35	4.29E-03	0.86	2.76E-02	2.81	1.87E-02	0.86	2.76E-02

SNORD100	48.98	15.58	1.77E-10	8.55	2.41E-05	12.12	2.77E-02	8.55	2.77E-02
KCNJ3	0.23	-1.34	4.64E-04	-0.71	2.65E-02	-1.33	2.79E-02	-0.71	2.79E-02
CD1E	52.15	4.01	1.05E-02	1.61	2.84E-02	4.87	8.62E-04	1.61	2.84E-02
PPA1	317.49	1.06	2.87E-02	0.87	3.08E-05	1.90	5.68E-06	0.87	2.87E-02
SLC24A2	0.14	-1.30	1.22E-02	-0.90	2.88E-02	-0.92	7.77E-03	-0.90	2.88E-02
MBD3	7.39	-2.51	1.71E-02	-1.15	8.57E-03	-1.61	2.89E-02	-1.15	2.89E-02
PRELID1	431.81	0.80	3.01E-04	0.57	1.98E-02	1.13	2.91E-02	0.57	2.91E-02
SRSF3	292.52	0.45	2.94E-02	0.55	1.27E-02	1.22	1.24E-03	0.45	2.94E-02
ASAP1	101.11	2.09	2.95E-02	1.35	2.07E-04	2.04	2.05E-02	1.35	2.95E-02
CAPZA1	262.11	1.00	2.98E-02	0.96	3.90E-03	0.86	2.09E-02	0.86	2.98E-02
CDK5RAP1	10.46	-2.23	2.68E-02	-1.73	2.98E-02	-2.40	8.04E-03	-1.73	2.98E-02
TRPM6	0.04	-2.79	1.65E-03	-1.96	3.08E-02	-1.98	2.30E-02	-1.96	3.08E-02
RN7SL32P	0.03	-6.83	1.63E-04	-3.32	3.14E-02	-7.36	2.40E-03	-3.32	3.14E-02
DGKZ	3.03	-2.71	3.64E-05	-1.92	3.73E-05	-1.87	3.18E-02	-1.87	3.18E-02
ELMO1	181.98	1.80	1.62E-07	1.15	1.47E-04	1.81	3.18E-02	1.15	3.18E-02
ZDHHC17	28.06	1.04	2.09E-02	1.10	3.20E-02	2.75	6.77E-08	1.04	3.20E-02
STK4	148.91	2.09	3.21E-02	1.15	1.11E-04	2.24	4.46E-03	1.15	3.21E-02
ATP6AP1	123.35	0.90	3.22E-02	0.75	1.76E-02	0.91	1.58E-02	0.75	3.22E-02
PLEK	178.61	1.64	3.22E-02	0.73	5.49E-04	1.55	5.80E-07	0.73	3.22E-02
HAVCR2	79.19	1.38	3.23E-02	0.60	4.23E-03	1.86	2.26E-03	0.60	3.23E-02
C11orf76	0.29	-1.70	1.77E-02	-1.31	3.25E-02	-1.86	6.02E-04	-1.31	3.25E-02
STK17B	313.04	1.16	3.27E-02	0.74	1.62E-02	0.94	2.27E-04	0.74	3.27E-02
CNBP	487.37	0.53	3.28E-02	1.17	5.95E-04	1.67	5.79E-04	0.53	3.28E-02
WDR13	11.48	-2.56	1.35E-02	-1.47	5.03E-03	-2.32	3.29E-02	-1.47	3.29E-02
RRAS	0.19	-6.03	3.21E-02	-2.72	3.34E-02	-6.17	1.07E-02	-2.72	3.34E-02
CHCHD10	1.07	-4.16	3.41E-02	-3.20	2.20E-05	-5.17	3.59E-04	-3.20	3.41E-02
ESD	133.67	1.94	3.55E-04	0.75	2.16E-02	1.06	3.42E-02	0.75	3.42E-02
CCT5	112.57	0.72	3.25E-02	0.75	3.43E-02	1.90	8.64E-04	0.72	3.43E-02
COMMD9	105.37	0.76	6.10E-03	0.76	3.46E-02	1.95	6.57E-04	0.76	3.46E-02

RN7SL163P	0.04	-6.66	3.48E-02	-5.32	3.81E-04	-8.97	2.07E-05	-5.32	3.48E-02
CTSC	128.88	2.07	3.50E-02	0.81	4.79E-03	1.50	5.53E-03	0.81	3.50E-02
PDGFA	4.88	-0.97	5.78E-04	-0.66	3.51E-02	-1.15	1.63E-02	-0.66	3.51E-02
GAPT	85.61	1.74	3.33E-02	1.13	2.82E-02	1.13	3.54E-02	1.13	3.54E-02
PTPRC	398.37	0.82	3.54E-02	0.80	2.06E-03	1.46	6.73E-05	0.80	3.54E-02
TMEM154	15.29	2.45	3.55E-03	0.80	3.58E-02	1.45	2.80E-02	0.80	3.58E-02
PCMT1	81.75	1.02	1.96E-02	1.01	7.18E-03	0.91	3.65E-02	0.91	3.65E-02
SLC43A3	13.67	-1.52	3.68E-02	-1.05	7.37E-03	-1.44	1.60E-03	-1.05	3.68E-02
SPIB	11.46	1.42	3.72E-02	1.23	1.93E-02	3.16	5.55E-06	1.23	3.72E-02
PSMA6	397.34	1.19	8.30E-03	0.60	2.25E-02	0.87	3.73E-02	0.60	3.73E-02
NT5DC1	15.33	3.33	7.35E-04	1.54	3.68E-02	2.33	3.74E-02	1.54	3.74E-02
ATP5I	114.89	-1.15	1.55E-02	-0.60	3.76E-02	-1.26	3.38E-03	-0.60	3.76E-02
BAZ2A	8.41	-1.58	3.77E-02	-1.48	1.56E-03	-1.53	2.73E-03	-1.48	3.77E-02
H2AFJ	52.38	-1.05	1.27E-02	-0.49	3.81E-02	-1.22	1.82E-02	-0.49	3.81E-02
HSF2	3.11	3.68	1.42E-02	2.70	1.14E-02	5.90	3.81E-02	2.70	3.81E-02
CD1C	1088.39	0.97	3.84E-02	1.11	2.70E-03	3.43	1.96E-03	0.97	3.84E-02
CCDC6	27.94	3.00	3.85E-02	0.85	1.02E-02	1.11	5.04E-05	0.85	3.85E-02
OAS3	21.89	3.86	4.10E-05	1.47	3.85E-02	1.25	1.31E-03	1.25	3.85E-02
SLC38A1	44.97	1.00	3.86E-02	0.58	3.07E-02	2.04	6.66E-03	0.58	3.86E-02
DBF4	15.30	2.74	1.12E-03	0.99	3.85E-02	2.27	3.87E-02	0.99	3.87E-02
PRR27	0.01	-4.56	1.69E-03	-2.04	3.89E-02	-3.51	2.22E-04	-2.04	3.89E-02
AP5Z1	2.51	-3.18	3.89E-02	-2.58	2.31E-03	-3.57	2.09E-03	-2.58	3.89E-02
LURAP1	0.02	-3.14	3.91E-02	-3.38	1.06E-03	-3.69	3.48E-04	-3.14	3.91E-02
ATP5F1	496.34	0.65	3.92E-02	0.88	1.24E-02	1.73	2.18E-03	0.65	3.92E-02
LGALS9	162.70	1.31	1.33E-02	0.74	1.13E-02	1.13	3.93E-02	0.74	3.93E-02
OR2V1	0.01	-7.41	3.96E-02	-3.30	9.31E-03	-4.77	7.64E-03	-3.30	3.96E-02
EMP3	123.56	-0.78	3.97E-02	-0.75	2.87E-03	-1.50	9.47E-08	-0.75	3.97E-02
TAB2	37.23	1.10	1.35E-02	0.52	4.03E-02	1.96	3.21E-03	0.52	4.03E-02
IDO1	3.36	1.28	2.44E-02	2.33	4.04E-02	4.46	3.21E-03	1.28	4.04E-02

CHD9	77.60	1.70	1.17E-02	0.88	1.83E-03	1.56	4.10E-02	0.88	4.10E-02
PABPC1	2105.31	0.59	4.15E-02	0.68	7.89E-03	1.00	1.54E-05	0.59	4.15E-02
FABP2	1.92	-1.68	5.35E-03	-1.02	2.41E-02	-1.26	4.16E-02	-1.02	4.16E-02
SCP2	118.32	1.41	1.25E-04	0.63	4.16E-02	1.31	1.11E-02	0.63	4.16E-02
FAM103A1	22.18	2.79	3.99E-04	0.98	3.82E-02	3.20	4.16E-02	0.98	4.16E-02
RABAC1	80.09	-1.10	8.60E-04	-0.51	4.17E-02	-1.22	5.49E-03	-0.51	4.17E-02
HDAC9	121.18	0.67	2.42E-03	0.85	1.01E-02	1.82	4.22E-02	0.67	4.22E-02
GAK	20.87	-1.52	4.23E-02	-1.63	1.12E-04	-1.94	2.38E-02	-1.52	4.23E-02
CST3	6747.21	0.93	1.04E-02	0.69	4.24E-02	1.46	2.44E-05	0.69	4.24E-02
TUBGCP2	32.63	-1.55	4.24E-02	-1.10	1.96E-03	-1.52	6.74E-03	-1.10	4.24E-02
GPM6A	0.78	-1.67	5.94E-03	-1.39	2.27E-03	-2.93	4.25E-02	-1.39	4.25E-02
RN7SL670P	0.15	-5.02	3.30E-02	-3.26	3.69E-02	-4.17	4.25E-02	-3.26	4.25E-02
NLRP12	0.67	-3.88	4.26E-02	-2.54	2.16E-04	-4.20	5.43E-07	-2.54	4.26E-02
MCOLN2	36.26	2.42	8.95E-03	1.90	1.13E-05	2.85	4.30E-02	1.90	4.30E-02
KIT	0.96	4.87	4.30E-02	3.73	4.03E-03	8.21	3.05E-06	3.73	4.30E-02
MIB2	0.46	-3.05	4.30E-02	-2.13	2.47E-02	-4.09	1.20E-02	-2.13	4.30E-02
TNFRSF1B	16.59	-1.32	4.32E-02	-1.57	1.90E-06	-2.27	1.55E-04	-1.32	4.32E-02
TMEM55A	54.33	3.55	4.32E-02	2.47	2.52E-04	5.08	9.90E-03	2.47	4.32E-02
SSBP4	7.78	-2.24	4.33E-02	-1.54	6.31E-04	-2.09	1.67E-02	-1.54	4.33E-02
BLNK	26.24	2.33	2.97E-02	2.19	2.36E-04	2.70	4.38E-02	2.19	4.38E-02
RANP1	0.01	2.71	5.09E-03	2.03	4.41E-02	2.71	5.09E-03	2.03	4.41E-02
MIR548AD	0.03	4.87	8.58E-03	4.10	4.41E-02	4.87	8.58E-03	4.10	4.41E-02
RN7SL25P	0.11	-6.32	2.74E-03	-2.53	4.42E-02	-4.30	1.14E-02	-2.53	4.42E-02
BTAF1	21.76	2.55	4.45E-02	1.02	4.61E-03	2.46	9.79E-04	1.02	4.45E-02
SYNE4	0.01	-4.51	4.45E-02	-2.92	8.57E-03	-3.12	1.51E-02	-2.92	4.45E-02
UFC1	195.10	1.17	4.48E-02	0.59	3.14E-03	2.13	1.86E-02	0.59	4.48E-02
RNA5SP395	0.01	2.59	4.48E-02	2.59	4.48E-02	2.59	4.48E-02	2.59	4.48E-02
TCEA3	5.48	5.83	4.50E-02	2.57	5.29E-03	4.48	1.69E-04	2.57	4.50E-02
UQCR11	135.10	-0.74	1.91E-06	-0.33	4.51E-02	-0.83	2.59E-03	-0.33	4.51E-02

ZNF483	0.45	-1.85	4.52E-02	-1.43	1.84E-02	-2.14	2.92E-03	-1.43	4.52E-02
RIPPLY3	0.06	-3.69	3.70E-04	-2.00	4.53E-02	-2.71	1.56E-02	-2.00	4.53E-02
SCUBE1	0.12	-3.37	1.14E-02	-1.99	2.54E-02	-4.29	4.54E-02	-1.99	4.54E-02
LCP1	349.04	0.87	4.56E-02	1.11	3.21E-04	1.47	5.08E-04	0.87	4.56E-02
ALG3	39.85	1.62	7.20E-03	1.11	4.19E-02	1.36	4.57E-02	1.11	4.57E-02
ARPC3	1063.21	0.80	5.73E-04	0.40	4.59E-02	0.91	3.88E-03	0.40	4.59E-02
RHBDL2	0.09	-2.70	9.09E-04	-1.63	3.75E-02	-2.20	4.59E-02	-1.63	4.59E-02
SNX21	0.09	-4.08	4.28E-02	-2.86	4.55E-02	-3.85	4.60E-02	-2.86	4.60E-02
EHF	1.17	7.28	4.64E-02	7.06	6.96E-05	7.91	8.30E-03	7.06	4.64E-02
RNPC3	17.11	2.61	2.18E-02	0.88	4.64E-02	1.60	1.15E-04	0.88	4.64E-02
MBOAT4	0.20	5.57	4.68E-02	3.09	1.97E-02	7.67	2.98E-07	3.09	4.68E-02
TGFBI	233.08	0.42	4.17E-02	0.67	4.70E-02	0.75	3.61E-02	0.42	4.70E-02
PRPF38A	24.09	2.62	4.73E-02	1.36	5.06E-03	1.13	4.04E-02	1.13	4.73E-02
FPGS	6.74	-2.22	7.69E-03	-1.50	6.23E-03	-1.33	4.77E-02	-1.33	4.77E-02
PPP1R14B	1.01	-3.40	4.77E-02	-2.74	8.07E-04	-3.04	5.79E-04	-2.74	4.77E-02
GYPC	25.55	2.09	2.60E-03	0.75	4.78E-02	3.01	8.94E-03	0.75	4.78E-02
ACER3	51.91	2.26	2.89E-02	0.89	4.79E-02	2.12	3.00E-06	0.89	4.79E-02
UNC93B1	5.05	-1.82	4.80E-02	-1.39	5.10E-03	-2.92	4.93E-07	-1.39	4.80E-02
GPR160	19.73	2.32	4.81E-02	1.81	9.73E-04	2.23	2.54E-02	1.81	4.81E-02
CACNA2D3	60.08	2.41	4.23E-03	0.93	4.81E-02	2.47	4.35E-03	0.93	4.81E-02
TSPO	405.39	-0.55	4.83E-02	-0.56	1.59E-02	-1.21	6.94E-03	-0.55	4.83E-02
SRSF6	63.05	1.00	3.41E-02	0.73	1.87E-02	0.86	4.85E-02	0.73	4.85E-02
PLPP1	1.33	4.11	4.19E-02	2.86	8.39E-03	5.08	4.88E-02	2.86	4.88E-02
FAM117B	6.55	2.59	4.90E-02	0.89	3.08E-02	1.20	2.42E-02	0.89	4.90E-02
UBP1	18.87	1.92	4.91E-02	0.65	3.54E-02	1.01	2.68E-02	0.65	4.91E-02
MIR4502	0.01	2.68	4.95E-02	2.68	4.95E-02	2.68	4.95E-02	2.68	4.95E-02
SCARNA20	0.01	3.56	2.82E-02	3.04	4.99E-02	3.56	2.82E-02	3.04	4.99E-02

CD5-CD163- DC3 DEGs

geneSymbol	tpm.CD163-	lfc.CD5+	p.CD5+	lfc.CD14-	p.CD14-	lfc.CD14+	p.CD14+	lfc.MostConservative	p.MostConservative
SH2D4B	0.04	4.90	2.09E-06	4.13	1.02E-05	5.45	1.13E-04	4.13	1.13E-04
LRRC27	50.44	4.11	5.75E-07	4.49	3.94E-07	3.73	1.16E-04	3.73	1.16E-04
DIO3OS	4.92	9.02	1.92E-05	10.54	2.28E-05	9.67	2.15E-04	9.02	2.15E-04
ING4	82.42	2.72	2.43E-04	3.12	6.71E-06	1.72	9.29E-04	1.72	9.29E-04
PYDC1	1.98	10.28	3.67E-05	9.41	5.41E-05	10.95	1.45E-03	9.41	1.45E-03
DUSP22	15.76	-2.04	3.04E-04	-1.51	1.57E-03	-2.04	1.14E-03	-1.51	1.57E-03
DDX60	0.08	-6.36	3.44E-05	-5.46	7.31E-05	-6.79	1.61E-03	-5.46	1.61E-03
ATP10B	3.41	2.91	1.74E-04	2.99	1.50E-04	2.23	1.65E-03	2.23	1.65E-03
REXO1L1	12.25	5.71	2.73E-05	6.66	9.49E-06	4.88	1.99E-03	4.88	1.99E-03
THAP4	58.25	2.81	2.77E-06	3.95	8.20E-07	4.05	2.29E-03	2.81	2.29E-03
L3HYPDH	0.76	-3.87	7.66E-07	-3.01	8.71E-05	-4.33	2.51E-03	-3.01	2.51E-03
DDB1	94.63	1.29	8.61E-06	1.09	2.85E-07	1.86	2.66E-03	1.09	2.66E-03
OR4F17	25.20	2.85	1.62E-03	3.05	4.48E-04	2.52	3.01E-03	2.52	3.01E-03
TRIM34	0.53	-3.52	3.64E-03	-4.40	1.62E-03	-5.07	1.66E-03	-3.52	3.64E-03
WBSCR16	0.37	-2.94	3.76E-03	-3.27	2.10E-03	-4.61	9.71E-04	-2.94	3.76E-03
CLDN18	0.12	3.14	6.53E-04	3.68	2.17E-03	1.25	4.03E-03	1.25	4.03E-03
SMARCAD1	0.19	-5.01	2.79E-04	-3.19	4.04E-03	-4.28	3.30E-03	-3.19	4.04E-03
LINC00173	0.22	-3.83	4.66E-04	-4.70	5.47E-05	-3.91	4.44E-03	-3.83	4.44E-03
HELQ	0.20	-4.27	6.70E-06	-4.48	2.33E-06	-2.81	4.50E-03	-2.81	4.50E-03
CERS6	0.27	-3.18	1.21E-06	-3.15	1.26E-06	-4.21	4.75E-03	-3.15	4.75E-03
STK40	0.62	-2.96	5.17E-03	-3.39	2.05E-03	-3.68	2.80E-03	-2.96	5.17E-03
WSB1	43.86	-1.71	4.27E-05	-0.97	5.21E-03	-1.32	2.23E-03	-0.97	5.21E-03
PARP4	2.12	-2.67	7.52E-05	-2.66	1.63E-04	-2.09	5.39E-03	-2.09	5.39E-03
PPP1R18	7.83	-2.27	1.27E-03	-2.15	1.58E-03	-2.24	5.58E-03	-2.15	5.58E-03
FEM1C	0.73	-2.75	5.08E-06	-1.35	5.32E-03	-1.76	5.66E-03	-1.35	5.66E-03
ZHX1	2.01	-1.94	4.89E-05	-1.82	5.33E-05	-2.69	5.69E-03	-1.82	5.69E-03
SNX2	17.24	-2.30	1.01E-03	-2.28	2.40E-03	-1.97	5.95E-03	-1.97	5.95E-03

SRSF8	31.89	1.37	2.78E-03	1.95	4.87 E-05	3.08	6.05E-03	1.37	6.05E-03
YARS	6.64	-2.17	3.23E-03	-2.04	6.09 E-03	-2.14	4.26E-03	-2.04	6.09E-03
NEXN	0.23	-1.78	6.15E-03	-3.25	1.11 E-05	-4.59	3.12E-03	-1.78	6.15E-03
SESTD1	0.27	-5.29	2.83E-03	-4.59	6.60 E-03	-6.01	2.70E-03	-4.59	6.60E-03
OAS3	1.51	-3.86	4.10E-05	-2.38	2.36 E-03	-2.60	6.92E-03	-2.38	6.92E-03
HEMK1	0.50	-3.26	1.16E-03	-4.09	1.25 E-04	-4.50	7.15E-03	-3.26	7.15E-03
LGALS9C	0.22	4.39	2.71E-04	5.17	1.86 E-04	6.37	7.15E-03	4.39	7.15E-03
IGHG4	0.18	6.89	4.37E-09	4.89	5.59 E-04	5.90	7.47E-03	4.89	7.47E-03
KLHL12	0.21	-4.24	5.45E-04	-3.69	2.36 E-03	-4.00	7.71E-03	-3.69	7.71E-03
SNX10	18.71	-0.86	7.76E-03	-0.97	4.61 E-03	-1.64	5.29E-03	-0.86	7.76E-03
SSH2	10.44	-1.38	2.86E-04	-1.43	3.26 E-04	-1.78	7.79E-03	-1.38	7.79E-03
MAPK14	4.79	-2.11	7.99E-03	-2.26	6.38 E-03	-2.59	3.13E-03	-2.11	7.99E-03
PAF1	0.44	-3.60	8.10E-03	-4.34	1.77 E-03	-5.33	2.14E-03	-3.60	8.10E-03
ABCC8	2.52	8.52	3.68E-03	6.77	8.39 E-03	6.54	7.42E-03	6.54	8.39E-03
PAK1IP1	2.87	-2.58	8.84E-04	-1.81	5.35 E-03	-2.46	8.44E-03	-1.81	8.44E-03
AP4B1	1.09	-4.28	2.09E-03	-2.75	7.35 E-03	-3.32	8.45E-03	-2.75	8.45E-03
NOL6	0.24	-2.94	2.99E-03	-2.36	9.35 E-03	-3.75	6.30E-03	-2.36	9.35E-03
RPS2L1	0.34	5.20	2.13E-04	2.49	9.57 E-03	7.01	2.84E-03	2.49	9.57E-03
GFM2	1.65	-1.74	3.59E-03	-2.06	1.05 E-03	-3.20	1.01E-02	-1.74	1.01E-02
FAM53C	1.10	-2.92	3.90E-03	-2.69	8.22 E-03	-2.69	1.03E-02	-2.69	1.03E-02
DEC1	11.69	2.30	6.71E-04	1.56	5.31 E-03	2.26	1.03E-02	1.56	1.03E-02
RPS2P46	1.88	1.46	8.02E-03	1.48	1.04 E-02	1.58	3.42E-03	1.46	1.04E-02
RAET1K	0.50	6.90	1.05E-02	7.30	8.96 E-03	7.76	5.56E-03	6.90	1.05E-02
TMEM8A	0.13	-4.40	3.07E-04	-4.83	1.03 E-04	-5.90	1.15E-02	-4.40	1.15E-02
NOTCH3	4.13	5.54	1.41E-03	3.68	7.36 E-03	3.03	1.17E-02	3.03	1.17E-02
SLC35E2	0.75	-1.50	1.19E-02	-1.69	6.96 E-03	-2.36	7.53E-03	-1.50	1.19E-02
KIF13B	0.90	-1.72	1.44E-03	-2.02	6.76 E-05	-3.38	1.22E-02	-1.72	1.22E-02
DIO2	3.52	9.59	1.05E-02	8.54	1.26 E-02	11.01	7.82E-03	8.54	1.26E-02
SEMA3B	0.10	5.21	4.36E-03	4.18	1.26 E-02	5.51	6.62E-03	4.18	1.26E-02

ZNF33B	1.47	-1.84	1.49E-03	-1.83	1.81 E-03	-2.54	1.26E-02	-1.83	1.26E-02
ZCCHC9	0.61	-3.08	8.62E-05	-2.84	1.50 E-04	-2.67	1.30E-02	-2.67	1.30E-02
LRRC59	0.54	-3.39	2.14E-05	-3.88	4.25 E-06	-3.45	1.34E-02	-3.39	1.34E-02
COX7B	47.41	0.55	7.03E-03	0.50	1.11 E-02	0.72	1.37E-02	0.50	1.37E-02
ZNF148	1.23	-2.79	1.11E-02	-2.54	1.39 E-02	-3.28	6.84E-03	-2.54	1.39E-02
TREML3P	1.82	9.94	1.14E-02	8.29	1.39 E-02	10.83	1.18E-02	8.29	1.39E-02
C1GALT1C1	0.28	-3.82	3.89E-05	-2.47	2.11 E-03	-5.09	1.41E-02	-2.47	1.41E-02
TMEM131	1.36	-3.85	8.56E-05	-3.05	2.25 E-04	-2.04	1.42E-02	-2.04	1.42E-02
MORC4	14.58	1.70	3.65E-03	1.37	1.47 E-02	1.43	9.49E-03	1.37	1.47E-02
TMEM164	0.95	-1.96	1.48E-02	-2.58	5.28 E-03	-2.89	9.98E-03	-1.96	1.48E-02
WHAMMP2	6.88	1.42	1.48E-02	1.66	8.02 E-03	2.84	3.17E-03	1.42	1.48E-02
GAPDHP72	1.06	5.91	1.41E-03	3.47	1.44 E-02	5.52	1.50E-02	3.47	1.50E-02
ALKBH4	10.83	3.60	3.12E-03	1.95	1.50 E-02	3.25	1.64E-03	1.95	1.50E-02
SAFB2	64.41	2.24	7.88E-06	1.57	1.50 E-04	0.71	1.50E-02	0.71	1.50E-02
CGN	3.17	7.52	1.51E-02	7.68	1.35 E-02	8.25	1.16E-02	7.52	1.51E-02
TAF6	0.29	-3.42	1.52E-02	-3.41	1.37 E-02	-3.79	1.22E-02	-3.41	1.52E-02
DDX59	0.46	-3.68	5.08E-03	-4.45	1.43 E-03	-3.77	1.54E-02	-3.68	1.54E-02
C5orf17	10.61	3.45	1.01E-02	3.00	1.57 E-02	3.53	1.02E-02	3.00	1.57E-02
MMP2	2.72	10.70	1.60E-02	10.44	1.49 E-02	11.41	1.52E-02	10.44	1.60E-02
C11orf71	0.06	-4.77	6.89E-03	-4.30	1.65 E-02	-6.53	9.36E-03	-4.30	1.65E-02
ANKRD17	56.56	1.30	1.75E-03	1.69	1.77 E-04	1.72	1.66E-02	1.30	1.66E-02
OTUD7A	0.31	4.44	1.67E-02	3.87	1.63 E-02	5.62	5.06E-03	3.87	1.67E-02
PAIP2B	0.05	-2.32	3.85E-03	-2.81	1.88 E-04	-2.98	1.76E-02	-2.32	1.76E-02
FAM131A	15.25	5.83	3.66E-04	3.48	1.54 E-03	3.48	1.80E-02	3.48	1.80E-02
AASDHPPT	0.72	-4.25	2.05E-06	-3.77	1.16 E-05	-3.15	1.81E-02	-3.15	1.81E-02
HTATSF1	29.19	0.85	5.57E-05	2.18	1.19 E-04	2.92	1.87E-02	0.85	1.87E-02
LFNG	2.35	-1.66	4.93E-03	-1.76	3.18 E-03	-1.89	1.89E-02	-1.66	1.89E-02
ZDHHC12	80.48	2.03	2.00E-02	2.70	6.61 E-03	3.75	2.80E-03	2.03	2.00E-02
FAH	69.43	3.66	2.59E-03	2.02	2.01 E-02	4.63	1.57E-02	2.02	2.01E-02

CYFIP1	1.27	-3.61	4.76E-03	-3.25	9.51 E-03	-2.97	2.01E-02	-2.97	2.01E-02
SRSF4	52.92	0.81	1.09E-02	0.74	2.03 E-02	1.10	1.00E-02	0.74	2.03E-02
SCOC	0.34	-5.45	2.86E-07	-2.52	2.35 E-03	-3.24	2.05E-02	-2.52	2.05E-02
MAN1C1	21.33	5.38	1.13E-02	3.92	2.09 E-02	4.46	1.21E-02	3.92	2.09E-02
RPSA	1297.55	0.44	1.45E-02	0.66	2.11 E-02	0.66	4.50E-03	0.44	2.11E-02
PDGFC	0.02	-5.19	2.12E-02	-6.36	1.10 E-02	-9.31	6.23E-03	-5.19	2.12E-02
PREP	31.38	3.39	1.74E-02	3.86	1.26 E-02	3.29	2.14E-02	3.29	2.14E-02
RPL23AP2	3.27	1.21	4.95E-03	1.74	2.19 E-03	1.44	2.16E-02	1.21	2.16E-02
WDR66	6.56	1.43	1.10E-03	1.11	6.54 E-03	1.14	2.17E-02	1.11	2.17E-02
IFIH1	0.93	-2.98	4.37E-04	-2.06	5.22 E-03	-3.50	2.20E-02	-2.06	2.20E-02
EIF3S5P1	1.16	7.94	2.21E-02	8.07	2.17 E-02	10.18	1.62E-02	7.94	2.21E-02
SNX1	4.02	-3.07	3.67E-03	-2.41	1.54 E-02	-2.69	2.25E-02	-2.41	2.25E-02
CDH26	3.20	9.17	1.35E-02	7.42	2.17 E-02	6.60	2.30E-02	6.60	2.30E-02
IFITM3	117.80	-1.47	1.13E-02	-1.51	8.69 E-03	-2.10	2.31E-02	-1.47	2.31E-02
MAN1A2	2.77	-2.13	5.34E-07	-2.09	4.84 E-06	-1.91	2.31E-02	-1.91	2.31E-02
MUL1	0.03	-6.57	3.30E-04	-6.68	4.00 E-04	-4.81	2.32E-02	-4.81	2.32E-02
NECAB1	0.55	4.33	2.33E-02	4.35	1.95 E-02	5.40	1.28E-02	4.33	2.33E-02
NEK6	0.09	-2.78	7.24E-03	-2.88	4.34 E-03	-5.77	2.39E-02	-2.78	2.39E-02
SCLT1	7.48	-1.74	1.76E-04	-1.38	9.82 E-04	-1.16	2.42E-02	-1.16	2.42E-02
ZNF439	0.55	-2.74	7.74E-04	-2.12	8.19 E-03	-2.55	2.42E-02	-2.12	2.42E-02
IMMP1L	34.04	3.90	2.78E-03	2.42	1.23 E-02	5.44	2.44E-02	2.42	2.44E-02
ARHGDIG	4.93	8.41	6.77E-07	6.09	3.09 E-04	7.86	2.49E-02	6.09	2.49E-02
CCZ1B	99.76	1.56	2.46E-02	1.56	2.49 E-02	2.10	1.91E-02	1.56	2.49E-02
DEXI	12.66	3.12	8.65E-03	2.12	2.49 E-02	4.30	3.25E-03	2.12	2.49E-02
PNPLA8	2.55	-3.22	2.92E-03	-3.24	2.41 E-03	-3.04	2.52E-02	-3.04	2.52E-02
SHMT2	3.05	-2.57	2.86E-06	-2.42	6.12 E-07	-2.06	2.52E-02	-2.06	2.52E-02
ZNF493	19.79	1.82	1.30E-02	1.52	2.22 E-02	1.55	2.53E-02	1.52	2.53E-02
ANKAR	0.04	-4.54	2.30E-02	-3.83	2.54 E-02	-5.60	2.20E-02	-3.83	2.54E-02
PTPN4	18.06	1.85	2.57E-02	2.58	2.69 E-03	1.50	2.06E-02	1.50	2.57E-02

MYH11	13.72	4.11	1.67E-03	3.84	1.68 E-03	2.85	2.60E-02	2.85	2.60E-02
OR52E4	2.14	3.20	1.04E-02	3.49	1.03 E-02	3.40	2.64E-02	3.20	2.64E-02
MROH7	0.31	-0.88	2.73E-02	-1.49	2.43 E-03	-1.82	1.49E-02	-0.88	2.73E-02
GOLGA6L5	0.76	6.18	6.33E-03	4.51	2.73 E-02	7.76	1.51E-03	4.51	2.73E-02
TMEM144	0.50	-2.66	3.44E-04	-1.83	5.75 E-03	-4.70	2.74E-02	-1.83	2.74E-02
IVNS1ABP	12.89	-2.06	2.65E-02	-2.42	1.48 E-02	-2.15	2.82E-02	-2.06	2.82E-02
ACADM	6.82	-1.91	5.86E-04	-1.45	4.50 E-03	-2.03	2.82E-02	-1.45	2.82E-02
TRIO	12.12	-1.84	2.11E-02	-1.67	2.83 E-02	-1.78	2.66E-02	-1.67	2.83E-02
PDCD2	4.71	-2.43	3.78E-03	-2.02	7.94 E-03	-1.86	2.86E-02	-1.86	2.86E-02
RELA	48.61	2.00	5.18E-03	1.57	1.65 E-02	1.60	2.87E-02	1.57	2.87E-02
ATG4A	0.02	-5.51	2.88E-02	-7.28	1.21 E-02	-6.74	2.78E-02	-5.51	2.88E-02
MPP7	1.16	-4.15	8.41E-04	-3.04	4.39 E-03	-3.06	2.89E-02	-3.04	2.89E-02
TRIM66	0.19	-3.69	7.01E-05	-2.38	1.31 E-03	-2.23	2.89E-02	-2.23	2.89E-02
CCDC92	0.45	-1.96	2.36E-02	-1.90	2.91 E-02	-3.90	3.24E-03	-1.90	2.91E-02
IGKC	141.63	3.60	4.79E-03	3.24	6.62 E-03	2.61	2.92E-02	2.61	2.92E-02
FRG1CP	0.58	-3.85	3.32E-04	-2.43	5.90 E-03	-3.46	2.93E-02	-2.43	2.93E-02
NUP153	0.39	-2.69	2.93E-02	-2.96	2.49 E-02	-3.35	1.59E-02	-2.69	2.93E-02
ZNF280C	0.02	-4.33	1.32E-02	-3.58	2.99 E-02	-5.31	2.16E-02	-3.58	2.99E-02
SRP54	4.04	-3.14	1.25E-02	-2.47	2.99 E-02	-2.58	2.72E-02	-2.47	2.99E-02
IKBKG	29.38	4.23	1.16E-03	2.85	6.46 E-03	1.70	2.99E-02	1.70	2.99E-02
RASSF8	4.93	3.73	2.11E-02	3.37	2.70 E-02	3.04	3.06E-02	3.04	3.06E-02
GSN	176.65	0.72	6.62E-03	0.56	3.06 E-02	1.16	3.04E-03	0.56	3.06E-02
PCNX3	8.62	2.36	2.19E-02	2.03	3.09 E-02	2.44	2.77E-02	2.03	3.09E-02
MED13L	2.74	-2.41	1.53E-03	-2.40	1.89 E-03	-2.07	3.10E-02	-2.07	3.10E-02
ARIH2OS	0.13	-3.58	2.38E-02	-3.48	3.11 E-02	-6.33	2.73E-03	-3.48	3.11E-02
PPP2R2B	28.08	7.02	4.86E-03	6.32	4.64 E-03	3.19	3.12E-02	3.19	3.12E-02
MKNK1	7.45	-1.72	3.13E-02	-2.15	1.31 E-02	-2.68	3.99E-03	-1.72	3.13E-02
ABCB5	9.53	8.20	2.75E-02	7.36	3.15 E-02	7.24	2.71E-02	7.24	3.15E-02
GPATCH2	0.60	-2.74	1.37E-02	-2.93	1.22 E-02	-2.67	3.18E-02	-2.67	3.18E-02

LBHD1	0.06	-3.77	2.50E-02	-5.23	9.97E-03	-5.40	3.24E-02	-3.77	3.24E-02
DYNLT1	43.31	-1.47	1.69E-02	-1.27	2.71E-02	-1.46	3.25E-02	-1.27	3.25E-02
PCCB	2.13	-2.42	2.14E-03	-2.67	1.87E-03	-2.67	3.27E-02	-2.42	3.27E-02
GABRP	17.93	3.05	9.81E-03	4.91	3.29E-03	1.88	3.30E-02	1.88	3.30E-02
LY6E	33.98	-1.31	1.16E-02	-1.28	1.24E-02	-1.86	3.34E-02	-1.28	3.34E-02
PIGT	214.72	1.34	1.10E-03	1.37	1.19E-03	0.93	3.34E-02	0.93	3.34E-02
PNMAL1	0.49	3.00	7.62E-04	1.39	2.73E-02	3.47	3.37E-02	1.39	3.37E-02
NSMCE2	3.16	-3.00	3.65E-06	-2.53	2.03E-05	-2.39	3.37E-02	-2.39	3.37E-02
ARL17A	24.34	1.53	2.06E-02	1.30	3.32E-02	1.27	3.38E-02	1.27	3.38E-02
OVCH2	0.98	7.86	3.39E-02	8.32	3.06E-02	7.70	2.99E-02	7.70	3.39E-02
FRK	6.68	1.71	2.67E-02	1.59	3.39E-02	1.51	3.42E-02	1.51	3.42E-02
ZFP42	2.37	2.52	7.30E-03	1.79	2.26E-02	1.55	3.45E-02	1.55	3.45E-02
SLC35C1	22.23	5.27	3.03E-02	4.61	3.47E-02	6.96	1.24E-02	4.61	3.47E-02
SULT1E1	0.72	5.38	3.51E-02	5.98	2.65E-02	7.91	1.06E-02	5.38	3.51E-02
DTX3L	2.32	-2.41	5.96E-03	-2.13	1.27E-02	-2.09	3.52E-02	-2.09	3.52E-02
YPEL2	0.78	-2.00	1.85E-02	-2.82	2.84E-03	-3.19	3.53E-02	-2.00	3.53E-02
OTUD4	1.01	-2.89	2.16E-02	-2.56	3.55E-02	-3.23	1.78E-02	-2.56	3.55E-02
SLC35E2B	0.72	-2.20	2.09E-02	-2.41	1.48E-02	-2.34	3.56E-02	-2.20	3.56E-02
CALCOCO1	1.13	-2.32	3.57E-02	-3.20	1.52E-02	-3.05	3.17E-02	-2.32	3.57E-02
DUX4L26	2.00	7.89	3.59E-02	8.54	3.17E-02	7.74	3.20E-02	7.74	3.59E-02
MINOS1	116.93	0.57	1.11E-02	0.52	3.61E-02	0.58	1.41E-02	0.52	3.61E-02
FRRS1L	5.28	2.47	1.61E-02	1.91	2.98E-02	1.80	3.62E-02	1.80	3.62E-02
RN7SL477P	11.00	8.50	1.69E-02	6.60	3.62E-02	8.73	2.28E-02	6.60	3.62E-02
NANOS3	5.78	11.48	3.39E-02	11.41	3.42E-02	10.21	3.63E-02	10.21	3.63E-02
SSR3	44.52	-1.48	2.50E-02	-1.17	3.63E-02	-1.77	1.04E-02	-1.17	3.63E-02
TTC7A	2.63	-1.63	3.64E-02	-2.70	5.06E-03	-2.93	4.37E-03	-1.63	3.64E-02
XRN1	7.70	-2.45	2.25E-03	-2.18	7.29E-03	-1.51	3.66E-02	-1.51	3.66E-02
ELAVL3	1.65	8.46	1.78E-02	6.68	2.70E-02	6.80	3.69E-02	6.68	3.69E-02
ZMYND10	5.62	8.83	2.57E-02	7.41	3.69E-02	8.13	2.44E-02	7.41	3.69E-02

DESI2	0.85	-2.31	2.47E-02	-2.32	3.70 E-02	-3.49	8.84E-03	-2.31	3.70E-02
UBTF	23.13	2.52	2.29E-03	1.74	1.09 E-02	1.40	3.73E-02	1.40	3.73E-02
ARMT1	0.11	-5.39	2.12E-02	-4.76	2.83 E-02	-5.32	3.74E-02	-4.76	3.74E-02
ZNF324	5.80	4.29	3.27E-02	4.33	2.82 E-02	3.39	3.76E-02	3.39	3.76E-02
GTF2H2C	28.69	1.22	3.78E-02	1.76	3.53 E-03	2.66	8.32E-03	1.22	3.78E-02
KIF19	0.96	4.26	1.17E-02	5.80	2.81 E-03	3.90	3.80E-02	3.90	3.80E-02
VMP1	37.13	-1.10	1.64E-03	-0.95	4.60 E-03	-0.97	3.80E-02	-0.95	3.80E-02
TMOD3	4.19	-1.70	9.74E-05	-1.58	1.49 E-04	-2.42	3.83E-02	-1.58	3.83E-02
RYR2	4.21	10.61	1.07E-04	9.95	1.21 E-04	6.93	3.83E-02	6.93	3.83E-02
MZT2B	67.55	2.66	1.40E-04	1.90	5.27 E-03	0.90	3.84E-02	0.90	3.84E-02
RELB	37.53	3.23	1.52E-03	1.70	1.87 E-02	1.42	3.85E-02	1.42	3.85E-02
DUXAP9	5.17	6.26	2.46E-02	5.99	3.39 E-02	8.16	3.86E-02	5.99	3.86E-02
RF00156	41.32	11.35	2.02E-02	9.06	3.88 E-02	13.02	1.21E-02	9.06	3.88E-02
MREG	1.22	6.86	3.94E-02	7.63	3.16 E-02	7.76	2.48E-02	6.86	3.94E-02
GRIN2C	0.55	7.04	3.19E-02	6.39	3.94 E-02	7.34	2.75E-02	6.39	3.94E-02
SCGB3A2	32.62	5.68	1.05E-02	4.10	2.47 E-02	3.20	3.95E-02	3.20	3.95E-02
RNF175	0.06	-3.92	3.97E-02	-5.86	1.67 E-02	-6.40	1.97E-02	-3.92	3.97E-02
PEF1	5.00	-3.12	2.08E-03	-1.44	3.14 E-02	-1.81	3.98E-02	-1.44	3.98E-02
GALM	0.65	-2.53	5.75E-03	-2.67	9.01 E-03	-2.42	4.00E-02	-2.42	4.00E-02
USP18	0.01	-4.90	1.10E-02	-3.72	4.04 E-02	-6.02	3.80E-02	-3.72	4.04E-02
C17orf101	0.98	-2.68	4.04E-02	-3.76	1.22 E-02	-3.48	2.62E-02	-2.68	4.04E-02
DDX19B	1.85	-3.31	4.37E-03	-2.78	8.47 E-03	-2.67	4.05E-02	-2.67	4.05E-02
BUB3	5.20	-3.14	2.40E-02	-2.71	4.09 E-02	-2.96	3.51E-02	-2.71	4.09E-02
GTF3C3	4.64	-3.27	5.62E-03	-2.06	4.10 E-02	-2.39	2.72E-02	-2.06	4.10E-02
IGLL5	4.37	6.26	3.41E-02	5.54	4.02 E-02	6.24	4.13E-02	5.54	4.13E-02
SGPL1	1.20	-2.03	2.88E-04	-2.31	1.23 E-04	-2.04	4.16E-02	-2.03	4.16E-02
EXOC3L4	1.55	4.65	1.98E-02	5.47	1.09 E-02	5.35	4.16E-02	4.65	4.16E-02
APOL1	0.28	-2.77	1.92E-02	-2.26	4.17 E-02	-3.27	2.76E-02	-2.26	4.17E-02
MED27	0.38	-3.05	3.07E-02	-4.18	8.53 E-03	-4.02	4.18E-02	-3.05	4.18E-02

REC8	2.51	-2.62	5.35E-03	-1.63	1.91 E-02	-2.32	4.21E-02	-1.63	4.21E-02
PDE6D	65.28	2.05	4.48E-03	2.59	9.38 E-04	3.12	4.21E-02	2.05	4.21E-02
MTHFS	0.15	-6.86	1.38E-02	-5.31	4.21 E-02	-7.45	1.44E-02	-5.31	4.21E-02
OR2I1P	0.37	4.41	4.22E-02	5.49	2.25 E-02	7.64	7.49E-03	4.41	4.22E-02
KMT2C	73.41	1.08	3.64E-03	1.32	1.79 E-04	1.72	4.23E-02	1.08	4.23E-02
MAGI2	68.47	5.82	3.01E-02	4.63	4.27 E-02	5.43	3.06E-02	4.63	4.27E-02
USE1	6.09	-1.94	3.90E-02	-2.00	4.31 E-02	-2.69	1.83E-02	-1.94	4.31E-02
HSPA14	1.79	-2.14	6.21E-03	-1.63	2.08 E-02	-2.46	4.34E-02	-1.63	4.34E-02
C6orf132	3.30	2.29	3.41E-02	2.00	4.35 E-02	2.74	1.69E-02	2.00	4.35E-02
SLC25A38	0.57	-4.29	1.82E-04	-3.59	3.43 E-03	-3.95	4.36E-02	-3.59	4.36E-02
NHLRC3	5.70	-1.34	2.76E-03	-0.77	4.36 E-02	-1.64	3.28E-02	-0.77	4.36E-02
POLR2M	25.08	2.15	1.59E-02	2.26	5.43 E-03	2.97	4.37E-02	2.15	4.37E-02
TOR1B	0.05	-4.59	1.01E-02	-6.37	2.42 E-03	-5.30	4.39E-02	-4.59	4.39E-02
MOV10	4.37	-2.38	3.71E-02	-2.49	3.01 E-02	-2.50	4.42E-02	-2.38	4.42E-02
BTN3A1	4.95	-1.35	1.92E-02	-1.11	4.43 E-02	-2.06	3.03E-02	-1.11	4.43E-02
AGAP5	0.16	-2.21	9.02E-03	-2.15	7.85 E-03	-3.71	4.44E-02	-2.15	4.44E-02
ADA	1.80	-3.47	4.68E-05	-1.45	2.90 E-02	-2.47	4.45E-02	-1.45	4.45E-02
PPRC1	0.76	-3.46	1.06E-02	-3.53	1.40 E-02	-3.58	4.51E-02	-3.46	4.51E-02
CHMP1B2P	1.52	3.69	4.04E-02	3.68	4.51 E-02	4.65	2.70E-02	3.68	4.51E-02
TRMT13	0.30	-4.47	1.32E-03	-3.58	9.47 E-03	-4.21	4.58E-02	-3.58	4.58E-02
ARL8A	0.24	-2.40	4.59E-02	-3.36	1.65 E-02	-3.40	3.30E-02	-2.40	4.59E-02
TNFRSF17	0.83	5.68	7.23E-03	5.19	1.05 E-02	4.89	4.59E-02	4.89	4.59E-02
FANCA	36.95	5.13	1.58E-02	5.29	1.54 E-02	2.72	4.65E-02	2.72	4.65E-02
RPS2	2417.68	0.60	6.63E-03	0.76	4.66 E-02	0.53	4.59E-02	0.53	4.66E-02
PRSS23	4.55	1.69	1.84E-02	1.28	4.66 E-02	1.79	1.86E-02	1.28	4.66E-02
FAM26E	0.12	4.69	3.04E-02	4.66	3.17 E-02	4.54	4.71E-02	4.54	4.71E-02
D2HGDH	5.92	4.74	1.80E-02	3.80	3.53 E-02	2.77	4.72E-02	2.77	4.72E-02
MFN2	0.86	-1.77	2.42E-02	-2.22	2.03 E-02	-2.26	4.72E-02	-1.77	4.72E-02
ARHGAP10	1.16	-1.13	4.75E-02	-2.50	4.17 E-04	-2.53	3.28E-03	-1.13	4.75E-02

PECAM1	13.94	-1.16	4.78E-02	-1.26	4.57 E-02	-1.51	4.23E-02	-1.16	4.78E-02
DHX40	1.13	-2.55	1.33E-03	-1.74	7.07 E-03	-2.67	4.78E-02	-1.74	4.78E-02
SLC41A3	32.46	2.75	4.86E-02	2.75	4.06 E-02	2.73	3.60E-02	2.73	4.86E-02
MCF2L	1.94	4.24	2.81E-02	3.46	4.88 E-02	3.12	4.67E-02	3.12	4.88E-02
CASP2	1.54	-2.61	1.24E-06	-2.94	8.31 E-12	-1.94	4.92E-02	-1.94	4.92E-02
ANKRD44	30.09	-1.96	3.39E-04	-1.16	1.05 E-02	-1.03	4.96E-02	-1.03	4.96E-02
MTHFR	17.71	1.88	7.21E-03	1.04	4.98 E-02	1.39	3.67E-02	1.04	4.98E-02

CD163+CD14- DC3 DEGs

geneSymbol	tpm.CD14-	lfc.CD5+	p.CD5+	lfc.CD163-	p.CD163-	lfc.CD14+	p.CD14+	lfc.MostConservative	p.MostConservative
ZNF583	1.14	2.06	1.64E-02	2.11	4.13E-03	2.28	8.88E-03	2.06	1.64E-02
RN7SL846P	0.28	5.07	1.67E-02	8.24	5.60E-05	8.24	5.60E-05	5.07	1.67E-02
FZD8	0.01	2.01	1.86E-02	2.59	1.45E-03	2.59	1.45E-03	2.01	1.86E-02
DNMT3L	0.01	3.26	1.94E-02	3.26	1.94E-02	3.26	1.94E-02	3.26	1.94E-02
FBXO10	0.01	2.99	2.33E-02	3.57	1.01E-02	3.57	1.01E-02	2.99	2.33E-02
GTF2H4	0.76	2.89	2.49E-02	7.43	5.96E-03	2.86	2.35E-02	2.86	2.49E-02
PRG2	0.01	2.93	3.00E-02	3.62	1.19E-02	3.62	1.19E-02	2.93	3.00E-02
RN7SL478P	0.02	3.51	3.30E-02	4.90	3.28E-03	4.90	3.28E-03	3.51	3.30E-02
CTTNBP2	0.38	3.68	4.06E-02	6.05	3.41E-02	6.80	1.88E-03	3.68	4.06E-02
SMIM6	0.01	2.66	4.15E-02	3.13	1.70E-02	3.13	1.70E-02	2.66	4.15E-02
KDM1B	6.67	1.03	4.52E-02	1.29	2.75E-03	1.40	3.44E-02	1.03	4.52E-02
CD109	2.49	1.61	4.62E-02	3.23	1.03E-02	3.38	5.00E-04	1.61	4.62E-02
RN7SL385P	0.01	2.31	4.92E-02	2.31	4.92E-02	2.31	4.92E-02	2.31	4.92E-02

CD163+CD14+ DC3 DEGs

geneSymbol	tpm.CD14+	lfc.CD5+	p.CD5+	lfc.CD163-	p.CD163-	lfc.CD14-	p.CD14-	lfc.MostConservative	p.MostConservative
RNY1P11	3.07	8.35	1.24E-04	11.59	6.23E-05	8.19	7.67E-06	8.19	1.24E-04
RPS26P31	1.04	5.09	3.34E-04	10.02	2.51E-05	6.34	8.72E-06	5.09	3.34E-04
AFF3	4.69	-3.05	7.11E-08	-2.13	3.61E-04	-2.17	1.25E-05	-2.13	3.61E-04

RGS1	43.41	-3.01	1.30E-06	-2.47	2.46E-04	-1.83	5.30E-04	-1.83	5.30E-04
RN7SL414P	1.09	9.63	2.06E-04	10.09	5.93E-04	8.48	6.96E-05	8.48	5.93E-04
ITM2C	0.64	-4.05	9.71E-08	-2.45	9.37E-04	-2.90	2.24E-05	-2.45	9.37E-04
S100A9	7898.61	4.54	7.82E-06	1.55	1.36E-03	2.02	8.68E-05	1.55	1.36E-03
S100A8	235199	5.92	1.01E-05	1.65	1.41E-03	2.71	4.70E-05	1.65	1.41E-03
ACAP3	5.09	3.73	3.18E-06	2.48	1.57E-03	1.60	1.62E-03	1.60	1.62E-03
CLEC4E	45.28	4.90	1.13E-05	3.51	2.32E-03	2.50	5.52E-04	2.50	2.32E-03
CREM	6.43	-3.69	7.35E-05	-2.91	2.64E-03	-2.83	7.70E-04	-2.83	2.64E-03
TAX1BP1	27.20	-1.44	4.49E-04	-1.18	2.69E-03	-1.15	1.52E-03	-1.15	2.69E-03
CKAP4	4.41	5.71	2.21E-07	3.34	3.93E-03	2.41	1.54E-03	2.41	3.93E-03
LINC01272	18.16	3.44	1.60E-03	4.21	1.38E-03	2.90	3.99E-03	2.90	3.99E-03
UBE2N	8.82	-2.80	3.58E-04	-2.84	2.03E-03	-1.99	4.13E-03	-1.99	4.13E-03
PSTPIP1	135.80	1.42	1.06E-03	1.11	4.50E-03	1.19	4.00E-03	1.11	4.50E-03
CD300E	41.66	2.47	1.80E-05	3.12	4.58E-03	1.15	2.36E-03	1.15	4.58E-03
SPINT2	16.69	-3.13	1.49E-03	-3.43	3.77E-03	-2.46	4.76E-03	-2.46	4.76E-03
CYBB	71.72	1.69	1.06E-03	1.39	3.69E-03	1.33	5.24E-03	1.33	5.24E-03
HIGD1A	8.61	-2.86	3.64E-04	-2.99	5.15E-03	-2.12	5.48E-03	-2.12	5.48E-03
XIAP	1.80	-1.87	3.03E-03	-1.98	5.66E-03	-2.18	9.13E-04	-1.87	5.66E-03
CTSD	200.11	3.33	9.72E-07	1.86	5.69E-03	1.77	1.37E-04	1.77	5.69E-03
NAPRT	120.63	1.90	3.49E-05	1.16	1.42E-03	1.48	6.38E-03	1.16	6.38E-03
SLC4A3	0.06	-7.39	2.16E-13	-6.90	6.54E-03	-5.70	5.33E-09	-5.70	6.54E-03
IKBKE	23.68	8.15	1.95E-04	7.80	7.71E-04	3.69	6.63E-03	3.69	6.63E-03
YWHAZ	135.82	-1.21	1.01E-06	-0.57	6.71E-03	-0.61	2.39E-03	-0.57	6.71E-03
YPEL5	67.72	-1.44	6.25E-06	-0.96	4.55E-03	-0.72	6.86E-03	-0.72	6.86E-03
RETN	79.05	4.67	1.67E-05	1.58	7.04E-03	1.89	3.48E-03	1.58	7.04E-03
RAD1	0.78	-3.40	3.97E-04	-5.32	4.62E-03	-2.39	7.13E-03	-2.39	7.13E-03
SNRNP40	4.99	-3.27	1.47E-04	-3.43	7.15E-03	-2.12	6.01E-03	-2.12	7.15E-03
VCAN	254.33	3.32	1.41E-08	0.70	7.17E-03	1.19	2.65E-03	0.70	7.17E-03
CLIC2	3.89	-4.01	1.47E-11	-3.61	7.91E-03	-2.71	5.96E-08	-2.71	7.91E-03

DOK3	7.35	9.32	3.91E-04	6.81	8.15E-03	4.25	8.00E-03	4.25	8.15E-03
BAIAP2	4.81	-1.54	4.90E-03	-3.31	8.95E-03	-2.18	1.73E-04	-1.54	8.95E-03
ZNF629	0.57	4.44	4.60E-03	4.33	4.02E-03	3.89	1.02E-02	3.89	1.02E-02
ACTG1	591.32	-1.54	2.37E-06	-0.78	7.84E-03	-0.64	1.09E-02	-0.64	1.09E-02
LRRFIP1	93.99	-0.89	4.15E-03	-0.80	1.13E-02	-0.90	3.40E-03	-0.80	1.13E-02
SENP7	25.44	1.03	5.80E-03	0.89	1.13E-02	0.88	7.02E-03	0.88	1.13E-02
ZDHHC17	4.17	-2.75	6.77E-08	-1.71	1.20E-02	-1.65	3.27E-04	-1.65	1.20E-02
CYP27A1	1.32	7.99	1.21E-02	8.39	1.05E-02	7.80	1.18E-02	7.80	1.21E-02
CDC42EP2	0.17	4.91	5.29E-04	5.99	1.23E-02	4.25	2.87E-03	4.25	1.23E-02
TBCA	35.00	-1.20	2.35E-03	-1.52	1.22E-03	-0.84	1.28E-02	-0.84	1.28E-02
FCGR1A	54.54	6.16	9.73E-05	3.76	1.30E-02	2.76	1.02E-02	2.76	1.30E-02
CLEC4A	61.19	-2.47	1.69E-03	-2.04	4.81E-03	-1.56	1.32E-02	-1.56	1.32E-02
ITGAM	37.41	2.87	1.36E-04	3.83	1.33E-02	2.02	3.30E-03	2.02	1.33E-02
C1orf228	31.86	6.42	1.53E-04	2.43	9.64E-03	2.30	1.36E-02	2.30	1.36E-02
CHST15	4.45	8.20	1.69E-06	8.30	1.39E-02	6.35	2.72E-05	6.35	1.39E-02
PHAX	3.25	-2.08	6.54E-03	-3.61	1.42E-02	-2.35	3.99E-03	-2.08	1.42E-02
GNAS	130.66	-0.87	7.00E-04	-0.58	1.44E-02	-0.62	8.99E-03	-0.58	1.44E-02
UTP18	7.01	-1.78	6.18E-03	-2.44	8.62E-03	-1.51	1.44E-02	-1.51	1.44E-02
NDUFB7	269.24	0.85	1.37E-03	0.80	1.47E-02	0.93	6.29E-03	0.80	1.47E-02
RBM39	24939	-1.07	3.43E-08	-0.76	1.32E-02	-0.47	1.47E-02	-0.47	1.47E-02
CTNS	17.59	3.31	1.81E-03	6.57	1.50E-02	3.27	2.24E-04	3.27	1.50E-02
PTEN	22.99	-1.86	6.82E-04	-1.40	1.52E-02	-1.21	1.15E-02	-1.21	1.52E-02
SLAMF7	1.54	-4.80	1.56E-09	-1.63	1.54E-02	-1.44	1.10E-02	-1.44	1.54E-02
C16orf86	1.68	5.67	4.84E-03	7.50	4.14E-03	4.54	1.54E-02	4.54	1.54E-02
MAP3K6	26.02	4.31	6.98E-04	3.06	1.58E-02	3.47	4.14E-04	3.06	1.58E-02
MTR	1.30	-1.64	1.58E-02	-2.30	5.78E-03	-1.86	8.96E-03	-1.64	1.58E-02
CD74	4100.48	-2.26	2.30E-06	-0.93	1.61E-02	-1.09	1.48E-03	-0.93	1.61E-02
CFL1	59300	-1.61	4.72E-04	-1.21	6.14E-03	-0.86	1.62E-02	-0.86	1.62E-02
LAMP1	9.82	4.51	1.05E-05	1.60	1.63E-02	1.91	2.65E-03	1.60	1.63E-02

SGK1	72.41	-0.90	1.64E-02	-1.37	5.18E-03	-0.98	6.55E-03	-0.90	1.64E-02
CD1C	101.31	-3.43	1.96E-03	-2.46	1.65E-02	-2.32	1.17E-02	-2.32	1.65E-02
LILRB4	4.82	-3.04	3.30E-03	-2.51	1.57E-02	-2.31	1.69E-02	-2.31	1.69E-02
ARL4C	29.99	-2.18	8.93E-06	-1.82	1.75E-02	-1.52	2.54E-04	-1.52	1.75E-02
GDI2	95.80	-1.58	1.03E-04	-0.84	1.77E-02	-0.75	1.46E-02	-0.75	1.77E-02
IFI27L2	100.85	2.23	6.60E-05	1.00	1.81E-02	1.59	6.99E-04	1.00	1.81E-02
CDK2AP2	33.44	-1.31	2.86E-04	-1.65	6.03E-04	-0.73	1.85E-02	-0.73	1.85E-02
KMT2D	17.53	3.03	2.26E-04	2.76	5.78E-03	1.31	1.86E-02	1.31	1.86E-02
NCF1	119.49	2.00	3.40E-03	2.25	1.86E-02	1.72	6.49E-03	1.72	1.86E-02
SPAST	4.74	-0.90	5.49E-03	-1.70	4.06E-03	-0.71	1.86E-02	-0.71	1.86E-02
ELOB	211.09	1.20	1.26E-03	0.68	1.87E-02	0.94	5.01E-03	0.68	1.87E-02
FCER1A	348.19	-2.64	4.02E-03	-2.00	1.92E-02	-1.79	1.60E-02	-1.79	1.92E-02
TGIF1	38.46	-1.44	7.39E-06	-1.44	1.93E-02	-0.70	3.61E-03	-0.70	1.93E-02
S100A6	1726.87	1.44	3.04E-04	0.65	1.93E-02	0.93	1.12E-02	0.65	1.93E-02
ATHL1	14.83	5.82	3.86E-04	2.82	2.03E-02	2.49	1.12E-02	2.49	2.03E-02
C12orf75	1.04	-4.70	1.52E-05	-3.57	2.05E-02	-2.83	3.20E-03	-2.83	2.05E-02
EIF2S3	65.60	-1.22	2.42E-04	-0.71	2.08E-02	-0.68	1.40E-02	-0.68	2.08E-02
PARVB	2.16	-1.35	1.74E-03	-1.97	2.11E-02	-2.18	2.23E-05	-1.35	2.11E-02
PARP10	9.57	3.04	4.72E-03	2.85	2.11E-02	2.13	1.15E-02	2.13	2.11E-02
POLR3G	1.83	4.36	1.45E-02	5.44	2.13E-02	5.36	1.39E-02	4.36	2.13E-02
RN7SL1	143.27	2.25	1.78E-03	1.29	2.16E-02	1.54	1.05E-02	1.29	2.16E-02
MAFB	18.64	6.69	1.66E-04	4.33	1.61E-02	2.11	2.16E-02	2.11	2.16E-02
PHTF2	2.64	-2.11	5.15E-03	-1.94	1.77E-02	-1.63	2.26E-02	-1.63	2.26E-02
CCT5	30.15	-1.90	8.64E-04	-1.18	2.34E-02	-1.15	9.50E-03	-1.15	2.34E-02
PLCG1	0.80	6.25	7.34E-03	9.64	3.02E-03	4.91	2.39E-02	4.91	2.39E-02
CHMP4A	28.34	-2.41	1.10E-03	-1.85	2.41E-02	-2.02	4.60E-03	-1.85	2.41E-02
MAN1A1	0.88	-2.23	1.47E-02	-2.33	2.46E-02	-2.06	2.05E-02	-2.06	2.46E-02
C1orf162	276.57	-2.05	2.05E-06	-1.28	1.58E-03	-0.65	2.57E-02	-0.65	2.57E-02
CCDC50	7.85	-2.03	4.10E-03	-2.21	4.90E-03	-1.48	2.58E-02	-1.48	2.58E-02

TUSC2	22.60	1.35	2.63E-02	7.17	2.69E-02	1.16	2.24E-02	1.16	2.69E-02
CCDC114	0.21	3.81	1.34E-03	1.78	2.70E-02	2.86	8.63E-03	1.78	2.70E-02
LY96	80.69	0.97	2.39E-02	1.71	2.73E-02	1.00	2.31E-02	0.97	2.73E-02
MYBBP1A	9.84	1.86	7.13E-03	1.44	2.76E-02	1.95	1.38E-02	1.44	2.76E-02
LITAF	25.86	-2.92	3.32E-04	-2.45	6.11E-03	-1.45	2.79E-02	-1.45	2.79E-02
TMEM109	66.16	-1.30	2.21E-03	-1.82	4.51E-03	-0.73	2.79E-02	-0.73	2.79E-02
CYB561A3	4.42	-2.34	5.93E-06	-2.48	2.80E-02	-1.86	6.41E-05	-1.86	2.80E-02
NBR2	0.02	-5.73	3.06E-03	-5.33	2.82E-02	-4.62	8.55E-03	-4.62	2.82E-02
CYC1	106.49	-1.06	3.43E-04	-0.92	2.86E-02	-0.85	2.53E-03	-0.85	2.86E-02
IL18	13.08	-2.81	2.40E-03	-2.43	1.19E-02	-1.87	2.89E-02	-1.87	2.89E-02
KDM6B	33.12	2.41	5.36E-03	3.16	1.04E-02	1.69	2.91E-02	1.69	2.91E-02
SRSF3	125.15	-1.22	1.24E-03	-0.78	2.55E-02	-0.68	2.93E-02	-0.68	2.93E-02
COMMD9	27.30	-1.95	6.57E-04	-1.19	3.00E-02	-1.18	1.93E-02	-1.18	3.00E-02
CCDC92	6.65	1.94	3.02E-02	3.90	3.24E-03	2.00	2.88E-02	1.94	3.02E-02
NFE2L1	8.28	2.62	4.11E-04	2.31	3.04E-02	1.74	1.82E-03	1.74	3.04E-02
CD63	390.16	1.27	2.87E-08	0.56	3.08E-02	0.79	1.22E-02	0.56	3.08E-02
CGREF1	0.13	5.83	6.00E-04	5.38	3.11E-02	4.35	6.22E-03	4.35	3.11E-02
SLC25A5	143.80	-1.81	2.00E-03	-1.65	3.22E-02	-1.20	2.72E-02	-1.20	3.22E-02
CCT2	42.26	-0.94	8.34E-04	-1.25	3.23E-02	-1.00	3.38E-04	-0.94	3.23E-02
PTBP3	9.19	-1.40	8.05E-03	-1.21	3.19E-02	-0.98	3.25E-02	-0.98	3.25E-02
CHPT1	4.72	-2.17	2.21E-03	-2.19	3.27E-02	-1.72	1.10E-02	-1.72	3.27E-02
HNRNPLL	1.61	-2.80	7.11E-03	-3.85	2.23E-02	-1.79	3.32E-02	-1.79	3.32E-02
UBL7	23.18	-1.89	3.56E-04	-1.88	1.94E-03	-0.96	3.33E-02	-0.96	3.33E-02
MIR7845	8.19	11.03	1.28E-05	13.00	3.46E-04	6.72	3.34E-02	6.72	3.34E-02
SPRED2	0.01	-4.24	2.99E-02	-5.50	2.87E-02	-3.98	3.36E-02	-3.98	3.36E-02
RPL3	1062.54	-0.86	5.29E-03	-0.89	6.49E-03	-0.56	3.41E-02	-0.56	3.41E-02
PTPN9	1.51	-2.52	6.50E-04	-2.69	3.44E-02	-1.52	1.99E-02	-1.52	3.44E-02
TK2	30.66	1.77	3.44E-02	1.52	2.04E-02	2.12	6.78E-03	1.52	3.44E-02
SH2B3	9.97	-2.56	1.02E-05	-1.63	3.44E-02	-1.53	1.37E-03	-1.53	3.44E-02

SUB1	191.45	-1.04	3.74E-04	-0.56	3.45E-02	-0.64	1.12E-02	-0.56	3.45E-02
CSNK2B	63.02	-1.78	1.54E-03	-1.18	3.45E-02	-1.10	1.73E-02	-1.10	3.45E-02
VPS33A	1.71	-2.27	1.69E-03	-2.02	3.47E-02	-2.32	1.46E-03	-2.02	3.47E-02
KIAA0513	5.36	2.22	1.80E-02	2.16	2.49E-02	1.79	3.48E-02	1.79	3.48E-02
GLG1	14.06	-1.44	2.15E-02	-1.46	2.48E-02	-1.25	3.53E-02	-1.25	3.53E-02
FOLR2	34.27	10.79	3.31E-04	6.93	3.53E-02	8.55	5.97E-04	6.93	3.53E-02
EMP3	350.50	1.50	9.47E-08	0.72	3.56E-02	0.75	5.50E-03	0.72	3.56E-02
N4BP2L1	10.73	-2.01	1.91E-02	-2.49	2.66E-02	-1.85	3.59E-02	-1.85	3.59E-02
NONO	35.40	-1.95	2.73E-03	-1.44	3.59E-02	-1.24	2.41E-02	-1.24	3.59E-02
GRID1	0.42	5.51	1.85E-02	4.78	3.24E-02	4.31	3.63E-02	4.31	3.63E-02
PUM1	12.84	-1.59	1.58E-02	-1.87	9.33E-03	-1.31	3.64E-02	-1.31	3.64E-02
EDEM1	3.16	-3.24	8.42E-03	-2.87	2.56E-02	-2.54	3.66E-02	-2.54	3.66E-02
BRI3	131.94	1.85	5.31E-04	1.29	9.44E-03	0.75	3.67E-02	0.75	3.67E-02
IL1B	101.41	-1.70	1.65E-03	-1.41	3.69E-02	-1.44	4.16E-03	-1.41	3.69E-02
AGTRAP	307.73	2.33	1.03E-03	0.95	3.71E-02	1.48	1.35E-02	0.95	3.71E-02
C14orf145	0.56	-3.89	3.04E-08	-3.54	3.74E-02	-2.90	1.91E-05	-2.90	3.74E-02
ST5	0.04	-5.44	2.37E-02	-6.08	3.75E-02	-5.00	2.54E-02	-5.00	3.75E-02
THEM4	1.30	-3.55	8.18E-07	-2.50	3.77E-02	-1.92	1.41E-03	-1.92	3.77E-02
MFHAS1	4.98	3.41	2.43E-02	4.89	1.28E-02	3.49	3.77E-02	3.41	3.77E-02
ARIH2OS	10.68	2.75	3.78E-02	6.33	2.73E-03	2.85	3.01E-02	2.75	3.78E-02
ALS2CR12	4.68	4.67	2.01E-02	6.04	3.80E-02	3.62	3.21E-02	3.62	3.80E-02
DUT	21.29	-1.89	1.57E-04	-1.72	3.88E-02	-1.29	2.14E-03	-1.29	3.88E-02
NKRF	0.26	-3.65	2.87E-03	-4.30	3.88E-02	-2.44	2.70E-02	-2.44	3.88E-02
LGALS9B	0.86	7.73	1.69E-02	7.47	3.13E-02	5.98	3.89E-02	5.98	3.89E-02
RNMTL1	1.50	-1.92	1.04E-02	-2.67	3.90E-02	-1.66	3.35E-02	-1.66	3.90E-02
PPIF	17.87	-2.40	2.14E-04	-1.60	3.92E-02	-1.93	1.07E-03	-1.60	3.92E-02
SYNPO2	1.32	5.06	2.00E-02	3.59	3.97E-02	4.71	2.77E-02	3.59	3.97E-02
EIF4E3	7.44	4.21	6.30E-03	2.75	3.98E-02	3.08	1.49E-02	2.75	3.98E-02
UBE2L6	92.42	-1.53	1.25E-04	-1.13	2.83E-02	-0.65	4.00E-02	-0.65	4.00E-02

ACY1	0.40	-4.45	2.15E-02	-6.27	1.41E-02	-4.06	4.02E-02	-4.06	4.02E-02
OR6R2P	0.28	6.63	2.93E-02	8.15	1.74E-02	6.13	4.02E-02	6.13	4.02E-02
ARGLU1	89.61	0.34	4.04E-02	0.58	1.02E-02	0.94	1.10E-02	0.34	4.04E-02
FCGR3A	3.60	7.50	3.45E-02	6.03	4.04E-02	6.77	3.83E-02	6.03	4.04E-02
CACNB1	0.44	5.96	5.93E-03	7.32	4.82E-03	4.18	4.07E-02	4.18	4.07E-02
NNAT	0.05	4.39	3.60E-02	5.62	1.79E-02	4.20	4.07E-02	4.20	4.07E-02
GIMAP8	3.93	4.66	1.90E-02	6.23	1.48E-02	3.77	4.12E-02	3.77	4.12E-02
MALT1	6.80	-1.54	2.10E-02	-1.66	4.16E-02	-1.40	3.28E-02	-1.40	4.16E-02
ANKRD13A	10.60	-1.12	2.22E-03	-1.36	4.17E-02	-0.92	5.96E-03	-0.92	4.17E-02
DHRS7B	19.01	3.07	3.19E-02	3.32	2.15E-02	2.57	4.18E-02	2.57	4.18E-02
MANBA	20.44	-1.23	3.81E-04	-1.49	4.18E-02	-1.16	3.03E-04	-1.16	4.18E-02
VPS54	1.41	-2.27	4.22E-02	-3.28	2.59E-02	-2.42	4.14E-02	-2.27	4.22E-02
NUDT1	35.17	-1.03	4.30E-03	-1.25	4.23E-02	-0.96	6.78E-03	-0.96	4.23E-02
CIITA	51.31	-1.45	1.03E-02	-1.22	4.24E-02	-1.19	2.18E-02	-1.19	4.24E-02
FAM198B	8.60	5.31	3.05E-06	3.06	4.24E-02	2.27	3.62E-03	2.27	4.24E-02
SMIM4	26.75	2.79	1.10E-03	2.81	2.85E-02	1.21	4.27E-02	1.21	4.27E-02
HIC2	1.40	3.45	6.45E-03	4.18	2.52E-02	1.26	4.33E-02	1.26	4.33E-02
EVA1B	6.17	5.70	3.19E-03	5.85	2.81E-02	3.10	4.35E-02	3.10	4.35E-02
ATP5C1	116.68	-1.46	3.72E-03	-1.20	4.03E-02	-0.77	4.36E-02	-0.77	4.36E-02
AREG	16.68	-3.31	9.33E-03	-2.95	4.38E-02	-2.51	2.89E-02	-2.51	4.38E-02
STARD7	28.11	-0.92	7.87E-03	-1.04	4.39E-02	-0.76	2.01E-02	-0.76	4.39E-02
NEXMIF	0.13	4.85	1.27E-02	4.67	3.05E-02	3.37	4.46E-02	3.37	4.46E-02
ZNF865	0.05	2.83	7.48E-03	4.46	2.24E-02	2.30	4.50E-02	2.30	4.50E-02
RN7SL138P	12.88	7.25	2.77E-03	10.25	4.50E-02	5.11	1.85E-02	5.11	4.50E-02
NOG	1.57	1.57	1.11E-04	0.57	4.53E-02	0.85	1.15E-02	0.57	4.53E-02
SLC35F2	0.05	-6.56	1.41E-05	-3.42	4.54E-02	-4.28	2.16E-03	-3.42	4.54E-02
ALDH2	23.08	-2.09	5.40E-03	-1.47	4.54E-02	-1.45	3.73E-02	-1.45	4.54E-02
RN7SL113P	5.69	6.04	4.68E-02	9.82	1.03E-02	6.15	3.05E-02	6.04	4.68E-02
PDE4B	4.89	-2.41	1.60E-03	-1.42	4.71E-02	-1.84	6.88E-03	-1.42	4.71E-02

NDST2	19.98	2.43	3.51E-03	4.08	4.72E-02	1.18	2.75E-02	1.18	4.72E-02
SIGLEC16	2.42	6.36	1.64E-02	8.35	4.76E-02	5.92	2.11E-02	5.92	4.76E-02
MED22	8.42	2.43	2.22E-02	3.73	4.73E-02	1.97	4.79E-02	1.97	4.79E-02
APBB3	13.96	2.94	3.77E-02	6.78	1.05E-02	2.22	4.80E-02	2.22	4.80E-02
PNPT1	1.79	-2.78	5.05E-08	-2.75	4.88E-02	-2.11	1.30E-05	-2.11	4.88E-02
PCIF1	11.04	-1.49	2.75E-02	-2.27	5.33E-03	-1.25	4.90E-02	-1.25	4.90E-02
STAB1	115.39	7.37	2.12E-08	1.76	4.91E-02	2.50	5.32E-05	1.76	4.91E-02
TCTN2	1.46	1.60	4.93E-02	1.78	1.24E-02	1.42	3.62E-02	1.42	4.93E-02
OPHN1	2.47	-2.20	4.11E-03	-1.62	4.93E-02	-1.46	2.30E-02	-1.46	4.93E-02
PCBP2	96.84	-1.34	7.64E-04	-0.84	4.94E-02	-0.61	4.71E-02	-0.61	4.94E-02
C1QA	9.97	8.52	8.22E-04	13.28	8.53E-04	4.07	4.95E-02	4.07	4.95E-02
SLC11A1	28.46	4.24	3.45E-03	2.24	4.96E-02	1.93	3.79E-02	1.93	4.96E-02
EXTL2	0.05	-5.41	5.00E-02	-7.69	3.14E-02	-5.19	4.12E-02	-5.19	5.00E-02

Table S4 Clinical data FIG. 12A-D

ID	disease	Sex	Year of Birth	anti-dsDNA (IU/mL)	low compl e-ment	SLEDAI	Activity	Immunosuppressants
SLE1	SLE	F	1959	18	no	8	Arthritis, alopecia, dsDNA	Hydroxychloroquine
SLE2	SLE	F	1991	9.7	yes	6	Proteinuria (=class V), complement	Hydroxychloroquine
SLE3	SLE	F	1954	186	yes	4	complement, dsDNA	Hydroxychloroquine
SLE4	SLE	M	1977	8.5	no	0	none	Hydroxychloroquine
SLE5	SLE	F	1971	1.3	no	0	none	Prednisone 5, Azathioprine, Hydroxycloroquine
SLE6	SLE	F	1964	4.1	no	0	none	none
SLE7	SLE	F	1983	19	yes	4	dsDNA, complement	Prednisone 5, Azathioprine, Hydroxycloroquine

SLE8	SLE	F	1961	21	yes	5	complement, dsDNA, fever	colchicine, prednisone 5,
SLE9	SLE	F	1982	30	yes	6	complement, dsDNA, rash	Belimumab, Prednisone 7.5, Azathioprine, Colchicine, Hydroxychloroquine
SLE10	SLE	F	1981	52	yes	12	rash, arthritis, ulcers, dsDNA, complement	Prednisone 10, Hydroxychloroquine, MMF
dsSSC01	dSSc	F	1965	NA	NA	NA	NA	NA
dsSSC02	dSSc	M	1959	NA	NA	NA	NA	NA
dsSSC03	dSSc	NA	NA	NA	NA	NA	NA	NA
dsSSC04	dSSc	F	1979	NA	NA	NA	NA	NA
dsSSC05	dSSc	M	1978	NA	NA	NA	NA	NA
lsSSC01	LcSSc	F	1939	NA	NA	NA	NA	NA
lsSSC02	LcSSc	F	1977	NA	NA	NA	NA	NA
lsSSC03	LcSSc	F	1951	NA	NA	NA	NA	NA
lsSSC04	LcSSc	F	1967	NA	NA	NA	NA	NA
lsSSC05	LcSSc	F	1951	NA	NA	NA	NA	NA
eaSSC01	eaSSc	F	1969	NA	NA	NA	NA	NA
eaSSC02	eaSSc	F	1968	NA	NA	NA	NA	NA
eaSSC03	eaSSc	F	1977	NA	NA	NA	NA	NA
eaSSC04	eaSSc	F	1982	NA	NA	NA	NA	NA
eaSSC05	eaSSc	NA	1982	NA	NA	NA	NA	NA
Healthy 1	Healthy	F	1983	NA	NA	NA	NA	NA
Healthy 2	Healthy	F	1968	NA	NA	NA	NA	NA
Healthy 3	Healthy	F	1970	NA	NA	NA	NA	NA
Healthy 4	Healthy	F	1960	NA	NA	NA	NA	NA
Healthy 5	Healthy	F	1963	NA	NA	NA	NA	NA
Healthy 6	Healthy	F	1953	NA	NA	NA	NA	NA

Healthy 7	Healthy	F	1988	NA	NA	NA	NA	NA
Healthy 8	Healthy	F	1968	NA	NA	NA	NA	NA
Healthy 9	Healthy	NA	NA	NA	NA	NA	NA	NA
Healthy 10	Healthy	NA	NA	NA	NA	NA	NA	NA

Table S5 Clinical data FLT3L-inj

ID	disease	Sex	Year of Birth	treatment (FLT3L)
Flt-7003	FL*	M	1954	25ucg/kg daily days 1-5, 8-11
Flt-7004	FL	M	1954	25ucg/kg daily days 1-5, 8-11
Flt-7005	SLL**	M	1955	25ucg/kg daily days 1-5, 8-11
Flt-7008	FL	F	1963	25ucg/kg daily days 1-5, 8-11
Flt-7013	FL	M	1969	25ucg/kg daily days 1-5, 8-11
Flt-7014	FL	M	1960	25ucg/kg daily days 1-5, 8-11
Flt-7015	FL	F	1963	25ucg/kg daily days 1-5, 8-11

*follicular lymphoma (FL), **small lymphocytic lymphoma (SLL)

Flt-7006	FL	M	1973	25ucg/kg daily days 1-5, 8-11
Flt-7007	FL	F	1967	25ucg/kg daily days 1-5, 8-11

Table S6 Clinical data FIG. 14

ID	disease	Sex	Year of Birth	anti-dsDNA (IU/mL)	low com-plement	SLE DAI	Activity	Immunosuppressants
Serum-SLE001	SLE	F	1973	497	1	16	Active	HCQ*, Pred** 15, AZA***
Serum-SLE022	SLE	F	1974	109	1	4	Active	HCQ, Pred 5, AZA
Serum-SLE026	SLE	M	1958	131	1	8	Active	Pred 2.5, AZA
Serum-SLE037	SLE	F	1972	171	1	6	Active	HCQ, Pred 10, AZA
Serum-SLE078	SLE	F	1983	179	1	14	Active	HCQ, Pred 7.5, AZA
Serum-SLE109	SLE	F	1974	129	1	4	Active	Pred 5, AZA
Serum-SLE122	SLE	F	1958	281	1	8	Active	HCQ, Pred 2.5, AZA
Serum-SLE125	SLE	F	1983	269	1	20	Active	HCQ, Pred 7.5, AZA
Serum-SLE132	SLE	F	1991	116	1	20	Active	HCQ, Pred 2.5, AZA
Serum-SLE136	SLE	F	1979	111	1	6	Active	HCQ, Pred 5, AZA

Serum-SLE139	SLE	F	1988	173	1	6	Active	HCQ, Pred 10, MTX
Serum-SLE161	SLE	F	1993	1618	1	12	Active	HCQ, Pred 10,
Serum-SLE011	SLE	F	1978	1.8	0	0	Inactive	-
Serum-SLE016	SLE	F	1971	1.9	0	0	Inactive	HCQ, Pred 7.5, AZA
Serum-SLE027	SLE	F	1966	9.2	0	0	Inactive	HCQ
Serum-SLE040	SLE	F	1965	1.7	0	0	Inactive	-
Serum-SLE051	SLE	F	1961	10	0	0	Inactive	-
Serum-SLE059	SLE	F	1988	8.7	0	0	Inactive	HCQ, Pred 5, MMF
Serum-SLE060	SLE	F	1974	13	0	0	Inactive	HCQ, AZA
Serum-SLE084	SLE	F	1958	1	0	0	Inactive	-
Serum-SLE093	SLE	F	1993	1.3	0	0	Inactive	-
Serum-SLE099	SLE	F	1962	2.2	0	0	Inactive	-
Serum-SLE123	SLE	F	1984	5.4	0	0	Inactive	-
Serum-SLE155	SLE	F	1972	2	0	0	Inactive	-
Serum-SLE004	Healthy	F	1970	NA	NA	NA	NA	-
Serum-SLE012	Healthy	F	1966	NA	NA	NA	NA	-
Serum-SLE017	Healthy	F	1966	NA	NA	NA	NA	-
Serum-SLE019	Healthy	F	1065	NA	NA	NA	NA	-
Serum-SLE020	Healthy	F	1965	NA	NA	NA	NA	-
Serum-SLE034	Healthy	F	1969	NA	NA	NA	NA	-
Serum-SLE043	Healthy	F	1954	NA	NA	NA	NA	-
Serum-SLE058	Healthy	F	1976	NA	NA	NA	NA	-
Serum-SLE079	Healthy	F	1984	NA	NA	NA	NA	-
Serum-SLE120	Healthy	F	1964	NA	NA	NA	NA	-
Serum-SLE130	Healthy	F	1959	NA	NA	NA	NA	-
Serum-SLE147	Healthy	F	1985	NA	NA	NA	NA	-

*HCQ (Hydroxychloroquine), **Pred (Prednisone) ***AZA (Azathioprine)

Table S7 FACS antibodies

Target	Conjugate	Isotype	Clone	Provider
CADM1	Purified	chicken IgY	3E1	MBL
CD11b	Biotin	rat IgG2b	M1/70	BD Biosciences
CD303	Biotin	mouse IgG1	AC144	Miltenyi
CD14	BUV737	mouse IgG2a	M5E2	BD Biosciences
CD123	BUV395	mouse IgG2a	7G3	BD Biosciences
HLA-DR	BV785	mouse IgG2a	L243	Biolegend
CD5	BV711	mouse IgG1	UCHT2	BD Biosciences
CD135	BV711	mouse IgG1	4G8	BD Biosciences
CD3	BV650	mouse IgG1	SP34-2	BD Biosciences
CD14	BV650	mouse IgG2a	M5E2	BD Biosciences
CD16	BV650	mouse IgG1	3G8	BD Biosciences
CD19	BV650	mouse IgG1	SJ25C1	BD Biosciences
CD20	BV650	mouse IgG2b	2H7	BD Biosciences
CD11c	BV650	mouse IgG1	B-Ly6	BD Biosciences
CD163	BV605	mouse IgG1	GHI/61	Biolegend
CD45	V500	mouse IgG1	HI30	BD Biosciences

CD89	BV510	mouse IgG1	A59	BD Biosciences
CD1c	PercP/Cy5.5	mouse IgG1	L161	Biolegend
CD1c	BV421	mouse IgG1	L161	Biolegend
CD2	BV421	mouse IgG1	RPA-2.10	BD Biosciences
FceRIa	PerCP	mouse IgG2b	AER-37 (CRA-1)	Biolegend
IRF8	PercP/eFluor710	mouse IgG1	V3GYWCH	eBioscience
CD45RA	FITC	mouse IgG1	5H9	BD Biosciences
IKAROS	BV421	mouse IgG1	R32-1149	BD Biosciences
RelB	Alexa Fluor 488	rabbit IgG	EP613Y	Abcam
CD1c	PE/Cy7	mouse IgG1	L161	Biolegend
CD45RA	PE/Cy7	mouse IgG1	L48	BD Biosciences
CD88	PE/Cy7	mouse IgG2a	S5/1	Biolegend
CD33	PE/CF594	mouse IgG1	WM53	BD Biosciences
CD206	PE/CF594	mouse IgG1	19.2	BD Biosciences
CD268	PE/Dazzle594	mouse IgG1	11C1	Biolegend
CD169	PE	mouse IgG1	7-239	BD Biosciences
CD301	PE	mouse IgG2a	H037G3	Biolegend
IRF4	PE	rat IgG1	3E4	eBioscience
LAMP5	PE	mouse IgG1	124-40B	Biolegend
NOTCH2	PE	rat IgG1	16F11	eBioscience
CD16	APC/Cy7	mouse IgG1	3G8	Biolegend
FceRIa	APC/Cy7	mouse IgG2b	AER-37 (CRA-1)	Biolegend
CD14	AF700	Mouse IgG2a, κ	BM-16	Biolegend
CD34	AF700	mouse IgG1	581	BD Biosciences
PU.1	Alexa Fluor 647	mouse IgG1	7C6B05	Biolegend
CD89	APC	mouse IgG1	A59	Biolegend
CD141	APC	mouse IgG1	AD5-14H12	Miltenyi
KLF4	APC	goat IgG (polycll)	NA	R&D Systems

Table S8 FACS Panels

		Lazer	UV (355nm)	UV (355nm)	UV (355nm)	Violet (405nm)	Violet (405nm)	Violet (405nm)	Violet (405nm)	Violet(405nm)	Violet (405nm)	Blue (488nm)	Blue (488nm)	Yellow-green (561nm)	Yellow-green (561nm)	Yellow-green (561nm)	Red (640nm)	Red (640nm)	Red (640nm)
		detector	A	B	C	A	B	C	D	E	F	A	B	A	C	D	A	B	C
		Band pass filter	740/35	450/50	379/28	780/60	710/50	670/30	610/20	525/50	450/50	685/35	525/50	780/60	610/20	586/15	780/60	730/45	670/14
	Data in:	Cytometer (BD)																	
FLT3L-treated patients stainings	FIG. 4J	FORTESSA	BDCA2-biot+ Str-BUV737	L/D Blue	CD123 BUV395	HLA-DR BV786	CD135 BV711	CD3/14/19/20 BV650	CD11c BV605	CD45 V500	CD2 BV421	*IRF8 PP/eF710**	CD45RA FITC	CD1c PE/Cy7	CD33 PE/CF594	CD169 PE	CD16 APC/Cy7	CD34 AF700	CADM1+ a-Chk-AF647
FIG. 4D new markers validation panel	FIG. 4D	FORTESSA	CADM1+ a-chk-biot+ Str-BUV737	L/D Blue	CD123 BUV395	HLA-DR BV786	CD5 BV711	CD3/19/20 BV650	CD163 BV605	CD45 V500	CD1c BV421	FceRI PercP	CD45RA FITC	CD88 PE/Cy7	CD206 PE/CF594	CD301 PE	CD16 APC/Cy7	CD14 AF700	CD89 APC
PU.1 staining	FIG. 9G	FORTESSA	CADM1+ a-chk-biot+ Str-BUV737	L/D Blue	CD123 BUV395	HLA-DR BV786	CD5 BV711	CD3/19/20 BV650	CD163 BV605	CD45 V500	CD1c BV421	FceRI PercP	CD45RA FITC	CD88 PE/Cy7	CD206 PE/CF594	*LAMP5 PE*	CD16 APC/Cy7	CD14 AF700	*PU.1 AF647*
NOTCH2 KLF4 staining	FIG. 4L & FIG. 9G	FORTESSA	CADM1+ a-chk-biot+ Str-BUV737	L/D Blue	CD123 BUV395	HLA-DR BV786	CD5 BV711	CD3/19/20 BV650	CD163 BV605	CD45 V500	CD1c BV421	FceRI PercP	CD45RA FITC	CD88 PE/Cy7	CD206 PE/CF594	*NOTCH2 PE*	CD16 APC/Cy7	CD14 AF700	*KLF4 APC*
IRF4 IRF8 staining	FIG. 4L & FIG. 9G	FORTESSA	CD11biot+ str-BUV737	L/D Blue	CD123 BUV395	HLA-DR BV786	CD5 BV711	CD3/19/20 BV650	CD163 BV605	CD45 V500	CD1c BV421	*IRF8 PP/eF710*	CD45RA FITC	CD88 PE/Cy7	CD206 PE/CF594	*IRF4 PE*	CD16 APC/Cy7	CD14 AF700	*KLF4 APC*
IKAROS RelB IRF4 KLF4 staining	FIG. 9G	FORTESSA	CADM1+ a-chk-biot+ Str-BUV737	L/D Blue	CD123 BUV395	HLA-DR BV786	CD5 BV711	CD3/19/20 BV650	CD163 BV605	CD45 V500	*IKAROS BV421*	FceRI PercP	*RelB AF488*	CD45RA PE/Cy7	CD206 PE/CF594	*IRF4 PE*	CD16 APC/Cy7	CD14 AF700	*KLF4 APC*
Indexed-sorting panel	FIG. 7A & FIG. 6A-D	ARIAIII	CD11b-biot+ Str-BUV737	L/D Blue	CD123 BUV395	HLA-DR BV786	CD5 BV711	CD3/14/19/20 BV650	CD163 BV605	CD45 V500	CD1c BV421	FceRI PercP	CD45RA FITC	CD88 PE/Cy7	CD206 PE/CF594	CD169 PE	CD16 APC/Cy7	CD1a AF700	CD141 APC
Sort panel for cDC2 subsets bulk RNAseq	FIG. 10B-D,G & FIG. 12F-H	ARIAIII	CADM1+ a-chk-biot+ Str-BUV737	L/D Blue	CD123 BUV395	HLA-DR BV786	CD5 BV711	CD3/19/20 BV650	CD163 BV605	CD45 V500	CD1c BV421	FceRI PercP	CD45RA FITC	CD88 PE/Cy7	BAFF-R PE/Dazz94	CD169 PE	CD16 APC/Cy7	CD14 AF700	CD89 APC
Sort panel for cultures in serum & lunimex	FIG. 14A	FORTESSA		L/D Blue	CD123 BUV395	HLA-DR BV786	CD5 BV711	CD3/19/20 BV650	CD163 BV605	CD45 V500	CD1c BV421	FceRI PercP	CD45RA FITC	CD88 PE/Cy7		CD169 PE	CD16 APC/Cy7	CD14 AF700	CD141 APC
T cell proliferation and Ics panel	FIG. 10E	FORTESSA		L/D Blue				CD3 BV650	CD4, eVolve605		CellTrace Violet	CD8 PercP/Cy5.5	*IL-4 PE/Cy7*				*IFNg APC/eF780*		*IL-17A, eF660*

*Intracellular stainings are italized and in blue

Table S9 CyTOF antibodies

Metal_Marker	*Bar code
102Pd_BC*102	
103Rh_BC103	
104Pd_BC104	
106Pd_BC106	
108Pd_BC108	
110Pd_BC110	
112Cd_CD14	
141Pr_Clec12A	
142Nd_CD5	
143Nd_CD2	
144Nd_CD64	
145Nd_CD68	
146Nd_CD19	
146Nd_CD20	
146Nd_CD3	
147Sm_CD86	
148Nd_CD45RA	
149Sm_HLA-DR	
150Nd_CD80	
151Eu_CD141	
152Sm_CD1c	
153Eu_FcER1A	
154Sm_CD87	
155Gd_CD33	
156Gd_CD22	
157Gd_CXCR3	
158Gd_CD82	
159Tb_CD301	
160Gd_CD206	
161Dy_CD123	
162Dy_CD88	
163Dy_BTLA	
164Dy_CD89	
165Ho_CD71	
166Er_CD85d	
167Er_Integrin-B7	
168Er_CD26	
169Tm_CD163	
170Er_CD35	
171Yb_CD166	
172Yb_HLA-DQ	
173Yb_CD294	
174Yb_CD354	
175Lu_CD172b	
176Yb_CD11b	
209Bi_CD16	
89Y_CD45	

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APPLICATIONS

Human mononuclear phagocytes comprise phenotypically and functionally overlapping subsets of dendritic cells (DC) and monocytes, but their identification remains elusive. Embodiments of the method disclosed herein combined high dimensional protein and RNA expression data of human circulating DC and monocytes with machine-learning-based approaches to precisely delineate these cells and unravel their heterogeneity. Embodiments of the method clearly delineated monocytes from conventional DC2 (cDC2), and identified new markers including CD88/CD89 for monocytes and HLA-DQ/ FcεRIα for cDC2, allowing their unambiguous characterization in blood and tissues.

The disclosure also found that blood $CD1c^+CD163^+CD14^+$ pro-inflammatory cells were not monocytes but one of the four phenotypically and functionally distinct subsets contained in the broader cDC2 gate, and also related to the DC3 subpopulation defined by Villani *et al.* (Villani et al., 2017). Indeed, as shown in the disclosure, cDC2 can be subdivided into phenotypically and functionally distinct subsets based on CD5, CD163 and CD14 expression, including a unique subset of circulating inflammatory $CD5^-CD163^+CD14^+$ cells related to the previous defined DC3 subpopulation.

The relevance and importance of these cDC subsets was confirmed with the specific accumulation of $CD163^+$ DC3, which comprise $CD14^+$ DC3, in the blood of patients with systemic lupus erythematosus (SLE). These inflammatory DC3 were expanded in systemic lupus erythematosus patients, correlating with disease activity. At the transcriptional level, these cells exhibited a strong pro-inflammatory profile and functional activation features, including a strong capacity to prime naïve $CD4^+$ T cells towards Th2 and Th17 cells and secrete pro-inflammatory mediators that might contribute to disease physiopathology.

This disclosure offers new insights into MNP heterogeneity, clarifying the identification of monocyte vs cDC populations, as well as the heterogeneity of DC sub-populations in health and disease, thereby paving the way for the design of therapeutic strategies based on manipulating specific DC2 and DC3 subsets or specific DC subset-targeting therapies.

It will be appreciated by a person skilled in the art that other variations and/or modifications may be made to the embodiments disclosed herein without departing from the spirit or scope of the disclosure as broadly described. For example, in the description herein, features of different exemplary embodiments may be mixed, combined, interchanged, incorporated, adopted, modified, included etc. or the like across different exemplary embodiments. The present embodiments are, therefore, to be considered in all respects to be illustrative and not restrictive.

CLAIMS

1. A method of characterising dendritic cells, the method comprising:

determining an expression of one or more of CD5, CD14 and CD163 in the dendritic cells.

2. The method according to claim 1, wherein where the dendritic cells are determined to be $CD5^-$, $CD14^+$ and/or $CD163^+$, identifying the dendritic cells as pro-inflammatory dendritic cells.

3. The method according to any one of the preceding claims, wherein where the dendritic cells are determined to be $CD163^+CD14^+$, identifying the dendritic cells as highly pro-inflammatory dendritic cells that are more pro-inflammatory than $CD163^-$ or $CD14^-$ dendritic cells.

4. The method according to any one of the preceding claims, the method further comprising determining a proportion of $CD163^+CD14^+$ dendritic cells.

5. The method according to any one of the preceding claims, the method further comprising determining an expression of one or more of CD11b, CD36, CD64, CD87, CD107a, CD206, CD274, CD354, FcεRIα, HLA-DQ, CD2, CD59, CD81, CD166, CD229, CD271 and Integrin β7 in the dendritic cells.

6. The method according to any one of the preceding claims, wherein the dendritic cells have one or more of the following properties:

(i) is a conventional dendritic cell 2 (cDC2);

(ii) is dependent on IRF4 for differentiation;

(iii) is dependent on KLF4 for differentiation;

(iv) is dependent on FLT3 ligand (FLT3L) for differentiation; and

(v) is capable of activating and/or polarizing T cells.

7. A method of characterising inflammation and/or inflammatory disease in a subject, the method comprising:

determining a proportion of $CD5^-$, $CD14^+$, $CD163^+$, and/or $CD14^+CD163^+$ dendritic cells in the subject's sample,

wherein the proportion positively correlates with the level of inflammation and/or the severity of inflammatory disease in the subject.

8. The method according to claim 7, wherein where the proportion of $CD5^-$, $CD14^+$, $CD163^+$, and/or $CD14^+CD163^+$ dendritic cells in the subject's sample is greater than a threshold proportion derived from a control sample, identifying the presence of inflammation and/or inflammatory disease in the subject.

9. The method according to claim 7, wherein where the proportion of $CD5^-$, $CD14^+$, $CD163^+$, and/or $CD14^+CD163^+$ dendritic cells in the sample is greater than the proportion in an earlier sample from the same subject, identifying a worsening of inflammation and/or inflammatory disease in the subject, and

wherein where the proportion of $CD5^-$, $CD14^+$, $CD163^+$, and/or $CD14^+CD163^+$ dendritic cells in the sample is lower than the proportion in the earlier sample, identifying an improvement of inflammation and/or inflammatory disease in the subject.

10. The method according any one of claims 7-9, wherein the inflammatory disease is selected from the group consisting of systemic inflammatory disease, metabolic disorder, autoimmune disease and cancer.

11. The method according to claim 10, wherein the inflammatory disease is selected from the group consisting of inflammatory skin disease, inflammatory bowel diseases, asthma, acute respiratory distress

syndrome, chronic obstructive pulmonary disease, acute lung injury, bronchopulmonary dysplasia, cystic fibrosis, bronchitis, bronchiolitis, arthritis, osteoarthritis, ankylosing spondylitis and rheumatism.

12. The method according to claim 10, wherein the metabolic disorder is selected from the group consisting of obesity, diabetes satiety and endocrine deficiencies related to aging.

13. The method according to claim 10, wherein the autoimmune disease is selected from the group consisting of Systemic Lupus Erythematosus (SLE), diabetes, rheumatoid arthritis (RA), multiple sclerosis (MS), myasthenia gravis (MG), scleroderma, Crohn's disease, ulcerative colitis, Hashimoto's disease, Graves' disease, Sjögren's syndrome, polyendocrine failure, vitiligo, peripheral neuropathy, graft-versus-host disease, autoimmune polyglandular syndrome type I, acute glomerulonephritis, Addison's disease, adult-onset idiopathic hypoparathyroidism (AOIH), alopecia totalis, amyotrophic lateral sclerosis, ankylosing spondylitis, autoimmune aplastic anemia, autoimmune hemolytic anemia, Behcet's disease, Celiac disease, chronic active hepatitis, CREST syndrome, dermatomyositis, dilated cardiomyopathy, eosinophilia-myalgia syndrome, epidermolisis bullosa acquisita (EBA), giant cell arteritis, Goodpasture's syndrome, Guillain-Barré syndrome, hemochromatosis, Henoch-Schönlein purpura, idiopathic IgA nephropathy, insulin-dependent diabetes mellitus (IDDM), juvenile rheumatoid arthritis, Lambert-Eaton syndrome, linear IgA dermatosis, myocarditis, narcolepsy, necrotizing vasculitis, neonatal lupus syndrome (NLE), nephrotic syndrome, pemphigoid, pemphigus, polymyositis, primary sclerosing cholangitis, psoriasis, atopic dermatitis, rapidly-progressive glomerulonephritis (RPGN), Reiter's syndrome, stiff-man syndrome and thyroiditis.

14. The method according to claim 10, wherein the autoimmune disease is selected from the group consisting of psoriasis, atopic dermatitis, Systemic Lupus Erythematosus (SLE) and systemic sclerosis (SSc).

15. The method according to claim 10, wherein the cancer comprises a non-solid tumour, optionally wherein the non-solid tumor is selected from the group consisting of leukaemia, multiple myelomas and lymphomas.

16. The method according to claim 10, wherein the cancer comprises a solid tumor, optionally wherein the solid tumour comprises sarcoma and/or carcinoma, further optionally wherein the sarcoma and/or carcinoma is selected from the group consisting of hepatocellular carcinoma, fibrosarcoma, myxosarcoma, liposarcoma, chondrosarcoma, osteogenic sarcoma, chordoma, angiosarcoma, endotheliosarcoma, lymphangiosarcoma, lymphangioendotheliosarcoma, synovioma, mesothelioma, Ewing's tumor, leiomyosarcoma, rhabdomyosarcoma, colon carcinoma, pancreatic cancer, breast cancer, ovarian cancer, prostate cancer, squamous cell carcinoma, basal cell carcinoma, adenocarcinoma, sweat gland carcinoma, sebaceous gland carcinoma, papillary carcinoma, papillary adenocarcinomas, cystadenocarcinoma, medullary carcinoma, bronchogenic carcinoma, renal cell carcinoma, hepatoma, bile duct carcinoma, choriocarcinoma, seminoma, embryonal carcinoma, Wilms' tumor, cervical cancer, testicular tumor, lung carcinoma, small cell lung carcinoma, bladder carcinoma, epithelial carcinoma, glioma, astrocytoma, medulloblastoma, craniopharyngioma, ependymoma, pinealoma, hemangioblastoma, acoustic neuroma, oligodendroglioma, meningioma, melanoma, neuroblastoma, and retinoblastoma.

17. The method according to claim 10, wherein the cancer is selected from the group consisting of hepatocellular carcinoma, follicular lymphoma, small lymphocytic lymphoma, pancreatic tumour and breast cancer.

18. The method according to any one of claims 8-17, wherein where the presence and/or the worsening of inflammation and/or an inflammatory disease in the subject is identified, the method further comprises allocating the subject to an inflammatory disease treatment regimen.

19. The method according to claim 18, wherein the inflammatory disease treatment regimen comprises administering to the subject one or more agent selected from the group consisting of: an anti-inflammatory agent, an immunosuppressant agent, an anti-cancer agent, an inhibitor of FLT3L, an agent capable of binding to $CD5^-$, $CD14^+$, $CD163^+$, and/or $CD14^+CD163^+$ dendritic cells, an agent capable of neutralising $CD5^-$, $CD14^+$, $CD163^+$, and/or $CD14^+CD163^+$ dendritic cells, an antibody against $CD5^-$, $CD14^+$, $CD163^+$, and/or $CD14^+CD163^+$ dendritic cells, an agent capable of reducing the proportion of $CD5^-$, $CD14^+$, $CD163^+$, and/or $CD14^+CD163^+$ dendritic cells, an agent capable of reducing an activity of $CD5^-$, $CD14^+$, $CD163^+$, and/or $CD14^+CD163^+$ dendritic cells, an agent capable of reducing a number of a precursor of $CD5^-$, $CD14^+$, $CD163^+$, and/or $CD14^+CD163^+$ dendritic cells and an agent capable of inhibiting a differentiation of the precursor to $CD5^-$, $CD14^+$, $CD163^+$, and/or $CD14^+CD163^+$ dendritic cells.

20. A kit for characterising dendritic cells, inflammation and/or inflammatory disease, the kit comprising one or more reagent for detecting CD5, CD14 and/or CD163.