

## CLAIMS

1. A method of characterising a macrophage in a tissue of a subject, the method comprising

5 determining an expression of one or more biomarkers in the macrophage, wherein the one or more biomarkers is selected from the group consisting of Folr2, Serpina3i, Nid2, Slc27a6, Sema6a, Cdh13, Bcl6b, C6, Klf15, Marco, [CD209](#), ~~Cd209d~~, Tshz3, Bmpr1a, Tln2, Coro2b, Ackr2, 1110046J04Rik, Pcdhac2, Gm2253, Vsig4, Phactr1, Npr1, Cpne8, Angptl7, Gm26714, Aut2, Cxcl13, Sgce, 2900052N01Rik, ~~Cd209b~~, Timd4, ~~Cd209g~~, Mrc1 (CD206), Spp1, Il22ra2, Gm24112, Gm23010, Ighv7-1, Gm23628, Gm24620, Gm23058, Arhgef37, Gad1-ps, Gm26397, Ighv2-5, Chil3, Mir1934, 1810012K08Rik, Ighv1-59, Gm14119, Gm19620 and Snord71, [and](#)

[characterising the macrophage in the tissue to be a macrophage selected from the group consisting of an embryonic-derived macrophage, a long-lived tissue resident macrophage, and a monocyte-derived macrophage,](#)

15 [wherein where the macrophage is determined to express one or more of Folr2, Serpina3i, Nid2, Slc27a6, Sema6a, Cdh13, Bcl6b, C6, Klf15, Mrc1 \(CD206\), Marco, Cd209d, Tshz3, Bmpr1a, Tln2, Coro2b, Ackr2, 1110046J04Rik, Pcdhac2, Gm2253, Vsig4, Phactr1, Npr1, Cpne8, Angptl7, Gm26714, Aut2, Cxcl13, Sgce, 2900052N01Rik, Cd209b, Timd4 and Cd209g, the macrophage is identified as an embryonic-derived macrophage and/or a long-lived tissue resident macrophage, and](#)

20 [wherein where the macrophage is determined to express one or more of Spp1, Il22ra2, Gm24112, Gm23010, Ighv7-1, Gm23628, Gm24620, Gm23058, Arhgef37, Gad1-ps, Gm26397, Ighv2-5, Chil3, Mir1934, 1810012K08Rik, Ighv1-59, Gm14119, Gm19620 and Snord71, the macrophage is identified as a monocyte-derived macrophage.](#)

2. The method according to claim 1, wherein the method further comprises detecting the macrophage in the tissue by selecting cells that express one or more  
30 biomarkers selected from the group consisting of CD64, MerTK, Adgre1, CD11b, CD45, CD68, and CD163.

3. The method according to any one of the preceding claims, wherein the method further comprises determining the characteristics of the cells using t-SNE (T-distributed

Stochastic Neighbour Embedding (t-SNE)) and/or UMAP algorithm (Uniform Manifold Approximation and Projection).

~~4. The method according to any one of the preceding claims, wherein the macrophage is characterised based on its origin, optionally the method characterises the macrophage is an embryonic-derived macrophage, a long-lived tissue resident macrophage, and/or a monocyte-derived macrophage.~~

~~5. The method according to any one of the preceding claims, wherein where the macrophage is determined to express one or more of Folr2, Serpina3i, Nid2, Slc27a6, Sema6a, Cdh13, Bcl6b, C6, Klf15, Mrc1 (CD206), Marco, Cd209d, Tshz3, Bmpr1a, Tln2, Coro2b, Ackr2, 1110046J04Rik, Pcdhac2, Gm2253, Vsig4, Phactr1, Npr1, Cpne8, Angptl7, Gm26714, Auts2, Cxcl13, Sgce, 2900052N01Rik, Cd209b, Timd4 and Cd209g, the macrophage is identified as an embryonic-derived macrophage and/or a long-lived tissue resident macrophage.~~

64. The method according to any one of the preceding claims, wherein where the macrophage is determined to express one or more Folr2, CD206, CD209, and/or Timd4, the macrophage is identified as an embryonic-derived macrophage and/or a long-lived tissue resident macrophage.

~~7. The method according to any one of the preceding claims, wherein where the macrophage is determined to express one or more of Spp1, Il22ra2, Gm24112, Gm23010, Ighv7-1, Gm23628, Gm24620, Gm23058, Arhgef37, Gad1-ps, Gm26397, Ighv2-5, Chil3, Mir1934, 1810012K08Rik, Ighv1-59, Gm14119, Gm19620 and Snord71, the macrophage is identified as a monocyte-derived macrophage.~~

85. A method of diagnosing a disease in a subject in need thereof, wherein the method comprises

determining an expression of one or more of biomarkers selected from the group consisting of Folr2, Serpina3i, Nid2, Slc27a6, Sema6a, Cdh13, Bcl6b, C6, Klf15, Marco, ~~Cd209d~~, CD209, Tshz3, Bmpr1a, Tln2, Coro2b, Ackr2, 1110046J04Rik, Pcdhac2, Gm2253, Vsig4, Phactr1, Npr1, Cpne8, Angptl7, Gm26714, Auts2, Cxcl13, Sgce, 2900052N01Rik, ~~Cd209b~~, Timd4, ~~Cd209g~~, Mrc1 (CD206), Spp1, Il22ra2, Gm24112,

Gm23010, Ighv7-1, Gm23628, Gm24620, Gm23058, Arhgef37, Gad1-ps, Gm26397, Ighv2-5, Chil3, Mir1934, 1810012K08Rik, Ighv1-59, Gm14119, Gm19620 and Snord71 in a macrophage in a tissue obtained from the subject,

characterising the macrophages in the tissue to be one macrophage selected from the group consisting of an embryonic-derived macrophage, a long-lived tissue resident macrophage, and a monocyte-derived macrophage,

wherein the disease is an inflammation, an inflammatory disease, a metabolic disease, or a proliferative disease.

~~9. The method according to claim 8, wherein the method further comprising a method of providing immunotherapy to the subject based on the expression of the biomarkers.~~

~~10. The method according to claim 8 or 9, wherein the method characterises the macrophage in the tissue to be one macrophage selected from the group consisting of an embryonic-derived macrophage, a long-lived tissue resident macrophage, and a monocyte-derived macrophage.~~

~~11. The method according to any one of claims 8 to 10,~~

wherein where the macrophage is determined to express one or more of Folr2, Serpina3i, Nid2, Slc27a6, Sema6a, Cdh13, Bcl6b, C6, Klf15, Mrc1 (CD206), Marco, ~~Cd209d~~, CD209, Tshz3, Bmpr1a, Tln2, Coro2b, Ackr2, 1110046J04Rik, Pcdhac2, Gm2253, Vsig4, Phactr1, Npr1, Cpne8, Angptl7, Gm26714, Aut2, Cxcl13, Sgce, 2900052N01Rik, ~~Cd209b~~, Timd4 and ~~Cd209g~~, the macrophage is identified as an embryonic-derived macrophage and/or a long-lived tissue resident macrophage, ~~and~~

wherein where the macrophage is determined to express one or more of Spp1, Il22ra2, Gm24112, Gm23010, Ighv7-1, Gm23628, Gm24620, Gm23058, Arhgef37, Gad1-ps, Gm26397, Ighv2-5, Chil3, Mir1934, 1810012K08Rik, Ighv1-59, Gm14119, Gm19620 and Snord71, the macrophage is identified as a monocyte-derived macrophage, and

wherein the subject is diagnosed with the disease when:

an upregulation of one or more biomarkers selected from the group consisting of Folr2, Mrc1 (CD206), Marco, Vsig4, Fcna, Lyve1, Pla2g2d, Colec12, Cd163, A4galt, CD209, Ppp1r9a, P3h2, Cxcl13, Cd209f, Igkv 14-126, Timd4, Ric3, SrpX, Rxrg, Nrap,

Abcc9, Gm37248, Cpxm2, A230107N01Rik, and/or Igsf10 in an embryonic-derived macrophage and/or a long-lived tissue resident macrophage is detected; and/or an upregulation of one or more biomarkers selected from the group consisting of Spp1, IgKv12-38, Ngp, Ighv5-17, Cxcr, Pcdhb16, Pdyn, Ighg3, Igkv6-15, Ighv1-66, Chil3, Ly6c2, Rab44, and/or Ly6i in a monocyte-derived macrophage is detected.

~~126.~~ The method according to ~~any one of claims 8 to~~ claim 5-11, wherein where the macrophage is determined to express one or more Folr2, CD206, CD209, and/or Timd4, the macrophage is identified as an embryonic-derived macrophage and/or a long-lived tissue resident macrophage.

~~13. The method according to any one of the claims 8 to 12, wherein where the macrophage is determined to express one or more of Spp1, Il22ra2, Gm24112, Gm23010, Ighv7-1, Gm23628, Gm24620, Gm23058, Arhgef37, Gad1-ps, Gm26397, Ighv2-5, Chil3, Mir1934, 1810012K08Rik, Ighv1-59, Gm14119, Gm19620 and Snord71, the macrophage is identified as a monocyte-derived macrophage.~~

~~14. The method according to any one of the claims 8 to 13, wherein the subject is diagnosed with the disease when:~~

~~an upregulation of one or more biomarkers selected from the group consisting of Folr2, Mrc1 (CD206), Marco, Vsig4, Fcna, Lyve1, Pla2g2d, Colec12, Cd163, A4galt, Cd209d, Ppp1r9a, P3h2, Cxcl13, Cd209f, Igkv 14-126, Cd209g, Timd4, Ric3, SrpX, Rxrg, Nrap, Abcc9, Gm37248, Cpxm2, A230107N01Rik, and/or Igsf10 in an embryonic-derived macrophage and/or a long-lived tissue resident macrophage is detected; and/or an upregulation of one or more biomarkers selected from the group consisting of Spp1, IgKv12-38, Ngp, Ighv5-17, Cxcr, Pcdhb16, Pdyn, Ighg3, Igkv6-15, Ighv1-66, Chil3, Ly6c2, Rab44, and/or Ly6i in a monocyte-derived macrophages is detected.~~

~~15. The method according to any one of the claims 8 to 14, wherein the subject is diagnosed with the disease when:~~

~~an upregulation of one or more biomarkers selected from the group consisting of Folr2, Mrc1 (CD206), Marco, Vsig4, Fcna, Lyve1, Pla2g2d, Colec12, Cd163, A4galt, Cd209d, Ppp1r9a, P3h2, Cxcl13, Cd209f, Igkv 14-126, Cd209g, Timd4, Ric3, SrpX, Rxrg, Nrap, Abcc9, Gm37248, Cpxm2, A230107N01Rik, and/or Igsf10 in an embryonic-derived macrophage and/or a long-lived tissue resident macrophage is detected; and/or~~

~~an upregulation of one or more biomarkers selected from the group consisting of Spp1, Igkv12-38, Ngp, Ighv5-17, Cxcr, Pcdhb16, Pdyn, Ighg3, Igkv6-15, Ighv1-66, Chil3, Ly6c2, Rab44, and/or Ly6i in a monocyte-derived macrophage is detected.~~

5 ~~16. A method of treating a disease, comprising~~  
~~modulating a macrophage determined to express one or more biomarkers~~  
~~selected from the group consisting of Folr2, Serpina3i, Nid2, Slc27a6, Sema6a, Cdh13,~~  
~~Bcl6b, C6, Klf15, Marco, Cd209d, Tshz3, Bmpr1a, Tln2, Coro2b, Ackr2, 1110046J04Rik,~~  
~~Pcdhac2, Gm2253, Vsig4, Phactr1, Npr1, Cpne8, Angptl7, Gm26714, Aut2, Cxcl13,~~  
10 ~~Sgce, 2900052N01Rik, Cd209b, Timd4, Cd209g, Mrc1 (CD206), Spp1, Il22ra2,~~  
~~Gm24112, Gm23010, Ighv7-1, Gm23628, Gm24620, Gm23058, Arhgef37, Gad1-ps,~~  
~~Gm26397, Ighv2-5, Chil3, Mir1934, 1810012K08Rik, Ighv1-59, Gm14119, Gm19620~~  
~~and Snord71,~~  
~~wherein the disease is an inflammation, an inflammatory disease, a metabolic~~  
15 ~~disease, or a proliferative disease.~~

~~177.~~ A kit for characterising a macrophage, the kit comprising reagents for detecting  
one or more biomarker selected from the group consisting of Folr2, Serpina3i, Nid2,  
Slc27a6, Sema6a, Cdh13, Bcl6b, C6, Klf15, Marco, Cd209d, Tshz3, Bmpr1a, Tln2,  
20 Coro2b, Ackr2, 1110046J04Rik, Pcdhac2, Gm2253, Vsig4, Phactr1, Npr1, Cpne8,  
Angptl7, Gm26714, Aut2, Cxcl13, Sgce, 2900052N01Rik, ~~Cd209b,~~ Timd4,  
~~Cd209g,~~ CD209, Mrc1 (CD206), Spp1, Il22ra2, Gm24112, Gm23010, Ighv7-1,  
Gm23628, Gm24620, Gm23058, Arhgef37, Gad1-ps, Gm26397, Ighv2-5, Chil3,  
Mir1934, 1810012K08Rik, Ighv1-59, Gm14119, Gm19620 and Snord71.

25 wherein when used, the kit characterises the macrophage to be an embryonic-  
derived macrophage, a long-lived tissue resident macrophage, and/or a monocyte-  
derived macrophage.

~~188.~~ The kit of claim ~~177~~, wherein the kit comprises  
30 reagents for detecting an embryonic derived macrophage or a long lived tissue  
resident macrophage comprising one or more reagent for detecting one or more  
biomarker selected from the group consisting of Folr2, Serpina3i, Nid2, Slc27a6,  
Sema6a, Cdh13, Bcl6b, C6, Klf15, Mrc1 (CD206), Marco, ~~Cd209d,~~ CD209, Tshz3,  
Bmpr1a, Tln2, Coro2b, Ackr2, 1110046J04Rik, Pcdhac2, Gm2253, Vsig4, Phactr1,

Npr1, Cpne8, Angptl7, Gm26714, Aut5, Cxcl13, Sgce, [and](#) 2900052N01Rik, ~~Cd209b~~, Timd4, ~~and Cd209g~~, and/or

reagents for detecting a monocyte-derived macrophage comprising one or more reagent for detecting one or more biomarker selected from the group consisting of Spp1,

- 5 Il22ra2, Gm24112, Gm23010, Ighv7-1, Gm23628, Gm24620, Gm23058, Arhgef37, Gad1-ps, Gm26397, Ighv2-5, Chil3, Mir1934, 1810012K08Rik, Ighv1-59, Gm14119, Gm19620 and Snord71.