

CLAIMS

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

5 determining an expression of biomarkers in the macrophage populations, wherein the biomarkers are selected from the group consisting of Folr2, Serpina3i, Nid2, Slc27a6, Sema6a, Cdh13, Bcl6b, C6, Klf15, Marco, CD209, CD209a, CD209b, CD209c, CD209d, CD209e, CD209f, CD209g, Tshz3, Bmpr1a, Tln2, Coro2b, Ackr2, 1110046J04Rik, Pcdhac2, Gm2253, Vsig4, Phactr1, Npr1, Cpne8, Angptl7, Gm26714, 10 Aut2, Cxcl13, Sgce, 2900052N01Rik, Timd4, 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,

characterising the macrophage populations in the tumour tissue to be a macrophage population selected from the group consisting of an embryonic-derived 15 macrophage population, a long-lived tissue resident macrophage population, and a monocyte-derived macrophage population,

wherein where the macrophage population is determined to express Folr2, Serpina3i, Nid2, Slc27a6, Sema6a, Cdh13, Bcl6b, C6, Klf15, Mrc1 (CD206), Marco, CD209, CD209a, CD209c, CD209e, CD209f, Cd209d, Tshz3, Bmpr1a, Tln2, Coro2b, 20 Ackr2, 1110046J04Rik, Pcdhac2, Gm2253, Vsig4, Phactr1, Npr1, Cpne8, Angptl7, Gm26714, Aut2, Cxcl13, Sgce, 2900052N01Rik, Cd209b, Timd4 and Cd209g, the macrophage population is identified as an embryonic-derived macrophage population and a long-lived tissue resident macrophage population, and

wherein where the macrophage population is determined to express Spp1, 25 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 population.

30 2. The method according to claim 1, wherein the method further comprises detecting the macrophage populations in the tumour tissue by selecting cells that express 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).

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4. The method according to any one of the preceding claims, wherein where the macrophage population is determined to express Folr2, CD206, CD209, CD209a, CD209b, CD209c, CD209d, CD209e, CD209f, CD209g, and Timd4, the macrophage population is identified as an embryonic-derived macrophage population and a long-lived tissue resident macrophage population.

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

determining an expression of biomarkers selected from the group consisting of

15 Folr2, Serpina3i, Nid2, Slc27a6, Sema6a, Cdh13, Bcl6b, C6, Klf15, Marco, CD209, CD209a, CD209b, CD209c, CD209d, CD209e, CD209f, CD209g, Tshz3, Bmpr1a, Tln2, Coro2b, Ackr2, 1110046J04Rik, Pcdhac2, Gm2253, Vsig4, Phactr1, Npr1, Cpne8, Angptl7, Gm26714, Aut2, Cxcl13, Sgce, 2900052N01Rik, Timd4, 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 macrophage populations in a tumour tissue obtained from the subject,

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

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wherein where the macrophage population is determined to express Folr2, Serpina3i, Nid2, Slc27a6, Sema6a, Cdh13, Bcl6b, C6, Klf15, Mrc1 (CD206), Marco, CD209, CD209a, CD209b, CD209c, CD209d, CD209e, CD209f, CD209g, Tshz3, Bmpr1a, Tln2, Coro2b, Ackr2, 1110046J04Rik, Pcdhac2, Gm2253, Vsig4, Phactr1, Npr1, Cpne8, Angptl7, Gm26714, Aut2, Cxcl13, Sgce, 2900052N01Rik, and Timd4, the macrophage population is identified as an embryonic-derived macrophage population and a long-lived tissue resident macrophage population, and

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wherein where the macrophage population is determined to express Spp1, Il22ra2, Gm24112, Gm23010, Ighv7-1, Gm23628, Gm24620, Gm23058, Arhgef37,

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Gad1-ps, Gm26397, Ighv2-5, Chil3, Mir1934, 1810012K08Rik, Ighv1-59, Gm14119, Gm19620 and Snord71, the macrophage population is identified as a monocyte-derived macrophage population, and

wherein the subject is diagnosed with the disease when:

5 an upregulation of biomarkers selected from the group consisting of Folr2, Mrc1 (CD206), Marco, Vsig4, Fcna, Lyve1, Pla2g2d, Colec12, Cd163, A4galt, CD209, CD209a, CD209b, CD209c, CD209d, CD209e, CD209g, Ppp1r9a, P3h2, Cxcl13, Cd209f, Igkv 14-126, Timd4, Ric3, SrpX, Rxrg, Nrap, Abcc9, Gm37248, Cpxm2, A230107N01Rik, and Igsf10 in an embryonic-derived macrophage population and a
10 long-lived tissue resident macrophage population is detected; and/or

an upregulation of 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 Ly6i in a monocyte-derived macrophage population is detected,

wherein the upregulation of biomarkers is in reference to a healthy/normal tissue
15 adjacent to the tumour tissue, and

wherein the disease comprises liver tumour, pancreatic tumour, hepatocellular carcinoma, pancreatic ductal adenocarcinoma (PDAC), pancreatic adenocarcinoma, melanoma and/or breast cancer.

20 6. The method according to claim 5, wherein where the macrophage population is determined to express CD209a, CD209b, CD209c, CD209d, CD209e, CD209f, CD209g, Folr2, CD206, CD209, and Timd4, the macrophage population is identified as an embryonic-derived macrophage population and a long-lived tissue resident macrophage population.

25 7. A kit for characterising macrophage populations, the kit comprising reagents for detecting biomarkers selected from the group consisting of Folr2, Serpina3i, Nid2, Slc27a6, Sema6a, Cdh13, Bcl6b, C6, Klf15, Marco, Cd209d, CD209a, CD209b, CD209c, CD209e, CD209f, CD209g, Tshz3, Bmpr1a, Tln2, Coro2b, Ackr2,
30 1110046J04Rik, Pcdhac2, Gm2253, Vsig4, Phactr1, Npr1, Cpne8, Angptl7, Gm26714, Auts2, Cxcl13, Sgce, 2900052N01Rik, Timd4, 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,

wherein when used, the kit characterises the macrophage populations to be an embryonic-derived macrophage population, a long-lived tissue resident macrophage population, and a monocyte-derived macrophage population, wherein the kit comprises

- 5 reagents for detecting an embryonic derived macrophage population or a long lived tissue resident macrophage population comprising reagents for detecting biomarkers selected from the group consisting of Folr2, Serpina3i, Nid2, Slc27a6, Sema6a, Cdh13, Bcl6b, C6, Klf15, Mrc1 (CD206), Marco, CD209, CD209a, CD209b, CD209c, CD209d, CD209e, CD209f, CD209g, Tshz3, Bmpr1a, Tln2, Coro2b, Akr2,
 10 1110046J04Rik, Pcdhac2, Gm2253, Vsig4, Phactr1, Npr1, Cpne8, Angptl7, Gm26714, Auts2, Cxcl13, Sgce, and 2900052N01Rik, Timd4, and/or

- reagents for detecting a monocyte-derived macrophage population comprising reagents for detecting biomarkers selected from the group consisting of Spp1, Il22ra2, Gm24112, Gm23010, Ighv7-1, Gm23628, Gm24620, Gm23058, Arhgef37, Gad1-ps,
 15 Gm26397, Ighv2-5, Chil3, Mir1934, 1810012K08Rik, Ighv1-59, Gm14119, Gm19620 and Snord71.