[CLAIMS]

[Claim 1]

A proliferating macrophage-like cell (pMAC) that proliferates in a cytokine-dependent manner and is negative for CD14 and CD83.

[Claim 2]

The pMAC according to claim 1, wherein the cytokine is a granulocyte macrophage colony stimulating factor (GM-CSF) and/or a macrophage colony stimulating factor (M-CSF).

[Claim 3]

The pMAC according to claim 1 or 2, wherein a gene that inhibits a macrophage-like function is deleted or suppressed in expression.

[Claim 4]

The pMAC according to claim 3, wherein the aforementioned gene that inhibits a macrophage-like function is a signal regulatory protein α (SIRPα) gene.

[Claim 5]

The pMAC according to any one of claims 1 to 4, wherein the aforementioned pMAC further comprises a chimeric antigen receptor (CAR).

[Claim 6]

A method for producing a proliferating macrophage-like cell (pMAC), comprising a step of deleting a gene that inhibits a macrophage-like function or suppressing expression of the gene, and a step of expressing a gene that confers proliferating property.

[Claim 7]

The production method according to claim 6, comprising (1) a step of, in a pluripotent stem cell, deleting the gene that inhibits a macrophage-like function or suppressing expression of the gene, and then inducing differentiation into a myeloid cell to obtain a macrophage-like cell (MAC) (step 1), and

(2) a step of expressing the gene that confers proliferating property in the MAC obtained in step 1 to obtain a proliferating macrophage-like cell (pMAC) (step 2).

[Claim 8]

The production method according to claim 6, comprising (A) a step of expressing a gene that confers proliferating property in a myeloid cell differentiated from a pluripotent stem cell to obtain a proliferating myeloid cell (step A), and (B) a step of, in the proliferating myeloid cell obtained in step A, deleting the gene that inhibits a macrophage-like function or suppressing expression of the gene, and then inducing differentiation to obtain a proliferating macrophage-like cell (pMAC) (step B).

[Claim 9]

The production method according to any one of claims 6 to 8, wherein the gene that inhibits a macrophage-like function is a signal regulatory protein α (SIRPα) gene.

[Claim 10]

The production method according to any one of claims 6 to 9, wherein the gene that confers proliferating property is at least one type selected from the group consisting of c-MYC, BMI1 and MDM2.

[Claim 11]

A method for producing CAR-pMAC, comprising introducing a chimeric antigen receptor (CAR) into the pMAC obtained by the production method according to any one of claims 6 to 10.

[Claim 12]

A method for producing CAR-pMAC, comprising

(1) a step of, in a pluripotent stem cell, deleting the gene that inhibits a macrophage-like function or suppressing expression of the gene, and then inducing differentiation into a myeloid cell to obtain a macrophage-like cell (MAC) (step 1),

(2) a step of expressing the gene that confers proliferating property in the MAC obtained in step 1 to obtain a proliferating macrophage-like cell (pMAC) (step 2), and
(3) a step of introducing a chimeric antigen receptor (CAR) (step 3).

[Claim 13]

The production method according to claim 12, wherein the differentiation induction into the myeloid cell in step 1 is performed by the following method (i) or (ii).
(i) performing a layered culture of embryoid body (EB) induced from the pluripotent stem cells on feeder cells in a medium containing VEGF, and further culturing same in a medium containing VEGF, SCF, and TPO, or
(ii) performing a monolayer culture of embryoid body (EB) induced from the pluripotent stem cells in a medium containing BMP-4, VEGF, and SCF without feeder cells, and further culturing same in a medium containing VEGF, TPO, and GM-CSF.

[Claim 14]

The production method according to claim 13, wherein the induction from the pluripotent stem cell into the embryoid body (EB) is performed by the following methods (a) and (b):
(a) seeding pluripotent stem cells in a container for cell mass-forming culture to form an embryoid body (EB), wherein (b) the aforementioned container has fine spheroid wells at the bottom, and does not have a flat surface between adjacent wells.

[Claim 15]

A method for producing CAR-pMAC, comprising
(1) a step of, in a pluripotent stem cell, deleting the gene that inhibits a macrophage-like function or suppressing expression of the gene (step 1-1),

a step of seeding the pluripotent stem cell obtained in step 1-1, in which the gene that inhibits a macrophage-like function is deleted or expression of the gene is suppressed, in a container for cell mass-forming culture that has fine spheroid

wells at the bottom, and does not have a flat surface between adjacent wells, to form an embryoid body (EB) (step 1-2),

a step of obtaining a macrophage-like cell (MAC) by the following method (i) or (ii) from the EB obtained in step 1-2 (step 1-3),

(i) performing a layered culture of the aforementioned EB on feeder cells in a medium containing VEGF, and further culturing same in a medium containing VEGF, SCF, and TPO, or

(ii) performing a monolayer culture of the aforementioned EB in a medium containing BMP-4, VEGF, and SCF without feeder cells, and further culturing same in a medium containing VEGF, TPO, and GM-CSF,

(2) a step of expressing the gene that confers proliferating property in the MAC obtained in step 1-3 to obtain a proliferating macrophage-like cell (pMAC) (step 2), and

(3) a step of introducing a chimeric antigen receptor (CAR) into the pMAC obtained in step 2 to obtain CAR-pMAC (step 3).

[Claim 16]

The production method according to any one of claims 12 to 15, wherein the gene that inhibits a macrophage-like function is a signal regulatory protein α (SIRPα) gene.

[Claim 17]

The production method according to any one of claims 12 to 16, wherein the gene that confers proliferating property is at least one type selected from the group consisting of c-MYC, BMI1 and MDM2.

[Claim 18]

A proliferating macrophage-like cell that satisfies the following conditions when a main component analysis based on the gene expression profile obtained by performing a whole-transcriptome analysis using, as a comparison target, a cell population along the macrophage cell lineage consisting of an iPS cell-derived myeloid cell, an iPS cell-derived macrophage, a biologically derived monocyte cell, a biologically derived

macrophage M1, a biologically derived macrophage M2, and a biologically derived macrophage M0 is performed and the top two components with high contribution rates are selected as the analysis targets:

condition 1: no overlapping with plots of known macrophage cell lineages

condition 2: PC1 is 100 or more, and PC2 is plotted in the range of -80 to 0.

[Claim 19]

A pharmaceutical composition comprising the proliferating macrophage-like cell according to claim 5 and a pharmaceutically acceptable carrier.

[Claim 20]

The pharmaceutical composition according to claim 19, which is for treating at least one disease selected from the group consisting of a disease associated with a tumor or cancer, a neurodegenerative disease, an inflammatory disease, a cardiovascular disease, a fibrotic disease, and amyloidosis.