principal component analysis, of mouse pMAC, bone marrow-derived monocyte (BM-derived monocyte), bone marrow-derived macrophage M0 (BM-derived macrophages M0), mouse bone marrow-derived M1-type macrophage (BM-derived macrophages M1), mouse bone marrow-derived M2-type macrophage (BM-derived macrophages M2) and abdominal cavity-derived macrophage (Intraperitoneal macrophages), in which the first principal component (PC1: contribution rate 34%) is plotted on the horizontal axis, and the second principal component (PC2: contribution rate 21%) is plotted on the vertical axis. A closer distance between the plots of each cell shows that the gene expression profiles are more similar; conversely, a farther distance between the plots of each cell shows that the gene expression profiles are different.

[Fig. 2-1] Histograms showing the results of surface antigen analysis of CD11b, F4/80, CD16/32, CD64, I-A/E, and CD206 by flow cytometry of mouse bone marrow-derived monocyte (BM-derived monocyte), mouse intraperitoneal macrophage (Intraperitoneal macrophages), mouse bone marrow-derived macrophage (BM-derived macrophages M0), mouse bone marrow-derived M1-type macrophage (BM-derived macrophages M1), mouse bone marrow-derived M2-type macrophage (BM-derived macrophages M2) and mouse pMAC. The vertical axis indicates the percentage of cells present, and the horizontal axis indicates the fluorescence intensity of each measured marker.

[Fig. 2-2] A histogram showing the analysis results of surface antigens CD163, Ly6C, CD80, CD86, SiglecF and SIRPα by flow cytometry of mouse bone marrow-derived monocyte (BM-derived monocyte), mouse intraperitoneal macrophage (Intraperitoneal macrophages), mouse bone marrow-derived macrophage (BM-derived macrophages M0), mouse bone marrow-derived M1-type macrophage (BM-derived macrophages M1), mouse bone marrow-derived M2-type macrophage (BM-derived macrophage M2) and mouse pMAC. The vertical axis indicates the proportion

intensity is $1.00\times e^{10}$ (unit: p/sec/cm^2/sr). The vertical axis of the lower left line graph shows the total flux of luciferase luminescence (unit: 10^{10}photons/s), and the horizontal axis indicates the number of days after cancer cell transplantation. The vertical axis of the graph on the bottom right shows the mouse survival rate, and the horizontal axis shows the number of days after cancer cell transplantation. Cancer cell growth was observed in untreated mice, but in mice administered with CAR-pMAC-SIRPα-KO, the growth of cancer cells was suppressed by administration even after radiation exposure, and it was found that the progression of colorectal cancer peritoneal dissemination was suppressed to prolong the survival of individual mice.

[Fig. 17] A diagram showing the gene expression profile of each cell obtained by RNA sequencing analysis, followed by principal component analysis, of human pMAC, blood collection-derived CD14-positive cell-derived monocyte (CD14-derived monocyte), blood collection-derived CD14 positive cell-derived macrophage M0 (CD14-derived Macrophages M0), blood collection-derived CD14 positive cell-derived M1 type macrophage (CD14-derived Macrophages M1), blood collection-derived CD14 positive cell-derived M2 type macrophage (CD14-derived Macrophages M2), human iPS cell-derived myeloid cell (iPSC-derived Myeloid cells) and human iPS cell-derived macrophage (iPSC-derived macrophages), in which the first principal component (PC1: contribution rate 40%) is plotted on the horizontal axis, and the second principal component (PC2: contribution rate 18%) is plotted on the vertical axis. A closer distance between the plots of each cell shows that the gene expression profiles are more similar; conversely, a farther distance between the plots of each cell shows that the gene expression profiles are different. It can be seen that the gene expression profile of pMAC is vastly different from that of any known blood collection-derived or iPS cell-derived macrophages.

factors and the like, 0.2 ng/mL to 200 ng/mL is preferred, 2 ng/mL to 100 ng/mL is further preferred, and 5 ng/mL to 50 ng/mL is particularly preferred. The “medium free of VEGF” is a medium not supplemented with exogenous VEGF or a medium not containing exogenous VEGF.

[0050]

Similarly, as regards SCF, TPO, BMP-4, and GM-CSF, a medium containing SCF, TPO, BMP-4 and/or GM-CSF means a medium supplemented with exogenous SCF, TPO, BMP-4 and/or GM-CSF or a medium containing exogenous SCF, TPO, BMP-4 and/or GM-CSF. Therefore, while the dose of SCF, TPO, BMP-4 and/or GM-CSF may be influenced by other growth factors and the like, 0.2 ng/mL to 200 ng/mL is preferred, 2 ng/mL to 100 ng/mL is further preferred. In the case of TPO, it is more preferably 5 ng/mL to 15 ng/mL. In the cases of SCF, BMP-4 and GM-CSF, it is more preferably 5 ng/mL to 70 ng/mL.

[0051]

The “medium free of SCF, TPO, BMP-4 and/or GM-CSF” means a medium not supplemented with exogenous SCF, TPO, BMP-4 and/or GM-CSF or a medium not containing exogenous SCF, TPO, BMP-4 and/or GM-CSF.

[0052]

αMEM supplemented with 20% fetal bovine serum (FBS) can be used as a medium for mouse embryoid body in the present invention. Mouse mesenchymal C3H10T1/2 cells or mouse bone marrow-derived interstitial OP9 cells can be used as feeder cells. A completely synthetic medium, StemFit (Ajinomoto Co., Inc.), can be used as a medium for human embryoid body.

[0053]

As the medium, αMEM supplemented with 20% FBS and the like can be used.

[0054]

In the present invention, the “feeder cell” is other cell type used to adjust the culture conditions for undifferentiated maintenance culture and differentiation induction culture of iPS cells. Feeder cells that underwent mitomycin C treatment or

Step B' and step C' in this embodiment can be respectively performed in the same manner as step A and step B in embodiment 2 of the above-mentioned "production method of pMAC of the present invention" except that the CAR gene has been introduced in advance into the target cells.

[0074]

The introduction of a CAR gene into cells in step 3 in embodiment I and embodiment II, step 1' in embodiment III, and step A' in embodiment IV are described in detail below.

Chimeric antigen receptor (also referred to as CAR in the present specification)

CAR is a structure that contains, from the N-terminal side to the C-terminal side of a protein, a target-specific extracellular domain, a transmembrane domain, and an intracellular signal domain for effector functions of immune cells, and CAR gene is a gene encoding this receptor. The extracellular domain contains an antigen recognition site that exhibits target-specific binding. The transmembrane domain exists between the extracellular domain and the intracellular signal domain. The intracellular signal domain transmits signals necessary for immune cells to exert their effector functions. That is, when the extracellular domain binds to a target antigen, an intracellular signal domain is used that is capable of transmitting a signal necessary for activating immune cells.

[0075]

There have been several reports of experiments and clinical studies using CAR (e.g., Rossig C, et al. Mol Ther 10:5-18, 2004; Dotti G, et al. Hum Gene Ther 20:1229-1239, 2009; Ngo MC, et al. Hum Mol Genet 20 (R1):R93-99, 2011; Ahmed N, et al. Mol Ther 17:1779-1787, 2009; Pule MA, et al. Nat Med 14:1264-1270, 2008; Louis CU, et al. Blood 118:6050-6056, 2011; Kochenderfer JN, et al. Blood 116:4099-4102, 2010; Kochenderfer JN, et al. Blood 119:2709-2720, 2012; Porter DL, et al. N Engl J Med 365:725-733, 2011; Kalos M, et al. Sci Transl Med