CLAIMS

1. A method of producing polyploidized megakaryocytes, comprising forcing expression of an apoptosis suppressor gene in megakaryocytes before polyploidization, and culturing the cells.

2. The method according to claim 1, wherein the apoptosis suppressor gene is a BCL-XL gene.

3. The method according to claim 1 or 2, wherein in the culturing step, expression or function of a p53 gene product is inhibited.

4. The method according to any one of claims 1 to 3, wherein in the culturing step, the megakaryocytes before polyploidization are subjected to at least one of the following (a) to (c):

(a) treatment with an actomyosin complex function inhibitor;

(b) treatment with an ROCK inhibitor; and

(c) treatment with an HDAC inhibitor.

5. The method according to claim 4, wherein the ROCK inhibitor is Y27632; the HDAC inhibitor is valproic acid; and the actomyosin complex function inhibitor is blebbistatin.

6. The method according to any one of claims 1 to 5, wherein the culturing step is conducted at a temperature higher than 37°C.

7. The method according to any one of claims 1 to

6, wherein the megakaryocytes before polyploidization are obtained by forcing expression of an oncogene and any of the following genes (i) to (iii) in the cells at any differentiation stage from hematopoietic progenitor cells to megakaryocytes before polyploidization:

(i) a gene suppressing expression of a p16 gene or a p19 gene;

(ii) a gene suppressing expression of an Ink4a/Arf gene; and

(iii) a polycomb gene, and

culturing and proliferating the resulting cells.

8. The method according to claim 7, wherein a c-MYC gene is used as the oncogene and BMI1 is used as the any of the genes (i) to (iii).

9. The method according to claim 7 or 8, wherein the hematopoietic progenitor cells are derived from cells selected from the group consisting of iPS cells, ES cells, hematopoietic stem cells derived from cord blood, bone marrow blood, or peripheral blood, and hematopoietic stem cells.

10. A blood cell composition comprising the polyploidized megakaryocytes produced by the method according to any one of claims 1 to 9.

11. A method of producing a platelet, comprising:

obtaining polyploidized megakaryocytes by using the method according to any one of claims 1 to 9 and culturing the cells; and

collecting a platelet from the culture of the polyploidized megakaryocytes.

12. The method according to claim 11, wherein the step of culturing the polyploidized megakaryocytes is conducted while suppressing the expression of the apoptosis suppressor gene that has been forcibly expressed, or after the apoptosis suppressor gene is removed from the cells.

13. The method according to claim 11 or 12, wherein the step of culturing the polyploidized megakaryocytes is conducted in the absence of a serum and/or in the absence of a feeder cell.

14. The method according to any one of claims 11 to 13, wherein the step of culturing the polyploidized megakaryocytes is conducted from 1 day to 15 days.

15. The method according to any one of claims 11 to 14, wherein the step of culturing the polyploidized megakaryocytes is conducted at 37°C.

16. The method according to any one of claims 11 to 15, wherein in the step of culturing the polyploidized megakaryocytes, an ROCK inhibitor and/or an actomyosin complex function inhibitor is added to a medium.

17. The method according to claim 16, wherein the ROCK inhibitor is Y27632 and the actomyosin complex function inhibitor is blebbistatin.

18. A platelet produced by the method according to any one of claims 11 to 17.

19. A blood product comprising the platelet

according to claim 18.

CLAIMS

1. A method of producing polyploidized megakaryocytes, comprising the following steps:
forcing expression of an apoptosis suppressor gene in megakaryocytes before polyploidization wherein the megakaryocytes are obtained by forcing expression of an oncogene and any of the following genes (i) to (iii) in the cells at any differentiation stage from hematopoietic progenitor cells to megakaryocytes before polyploidization:

(i) a gene suppressing expression of a p16 gene or a p19 gene;

(ii) a gene suppressing expression of an Ink4a/Arf gene; and

(iii) a polycomb gene; and
culturing the cells.

2. The method according to claim 1, wherein the apoptosis suppressor gene is a BCL-XL gene.

3. The method according to claim 1 or 2, wherein in the culturing step, expression or function of a p53 gene product is inhibited.

4. The method according to any one of claims 1 to 3, wherein in the culturing step, the megakaryocytes before polyploidization are subjected to at least one of the following (a) to (c):

(a) treatment with an actomyosin complex function inhibitor;

(b) treatment with an ROCK inhibitor; and

(c) treatment with an HDAC inhibitor.

5. The method according to claim 4, wherein the ROCK inhibitor is Y27632; the HDAC inhibitor is valproic acid; and the actomyosin complex function inhibitor is blebbistatin.

6. The method according to any one of claims 1 to 5, wherein the culturing step is conducted at a temperature higher than 37°C.

7. The method according to any one of claims 1 to 6, wherein a c-MYC gene is used as the oncogene and BMI1 is used as the any of the genes (i) to (iii).

8. The method according to claim 6 or 7, wherein the hematopoietic progenitor cells are derived from cells selected from the group consisting of iPS cells, ES cells, hematopoietic stem cells derived from cord blood, bone marrow blood, or peripheral blood, and hematopoietic stem cells.

9. The method according to any one of claims 1 to 8, further comprising the step of suppressing the forced expression of the oncogene, the BMI1 gene and the BCL-XL gene.

10. A blood cell composition comprising the polyploidized megakaryocytes produced by the method according to any one of claims 1 to 9.

11. A method of producing a platelet, comprising:

obtaining polyploidized megakaryocytes by using the method according to any one of claims 1 to 9 and culturing

the cells; and

collecting a platelet from the culture of the polyploidized megakaryocytes.

12. The method according to claim 11, wherein the step of culturing the polyploidized megakaryocytes is conducted while suppressing the expression of the apoptosis suppressor gene that has been forcibly expressed, or after the apoptosis suppressor gene is removed from the cells.

13. The method according to claim 11 or 12, wherein the step of culturing the polyploidized megakaryocytes is conducted in the absence of a serum and/or in the absence of a feeder cell.

14. The method according to any one of claims 11 to 13, wherein the step of culturing the polyploidized megakaryocytes is conducted from 1 day to 15 days.

15. The method according to any one of claims 11 to 14, wherein the step of culturing the polyploidized megakaryocytes is conducted at 37°C.

16. The method according to any one of claims 11 to 15, wherein in the step of culturing the polyploidized megakaryocytes, an ROCK inhibitor and/or an actomyosin complex function inhibitor is added to a medium.

17. The method according to claim 16, wherein the ROCK inhibitor is Y27632 and the actomyosin complex function inhibitor is blebbistatin.

18. A platelet produced by the method according to any one of claims 11 to 17.

19. A blood product comprising the platelet according to claim 18.