Claims

1. A composition comprising an expanded population of cells for use in therapy, wherein the cells have been expanded by the method comprising;

i) obtaining an isolated population of HSPC

ii) culturing the isolated population of HSPC in the presence of a histone deacetylase inhibitor (HDAC inhibitor), to form a cultured population

iii) adding an aminothiol compound having the formula $RNH(C_nH_{2n})NH(C_nH_{2n})SX$, wherein R is hydrogen, an aryl, an acyl, or an alkyl group containing from 1 to 7 carbon atoms, each n has a value of from 2 to 6 and X is H or PO_3H_2; or a pharmaceutically acceptable salt thereof, to the cultured population of HSPC to form expanded cells.

2. The composition according to claim 1, for use in the treatment of a haematological disorder, immune disorder, metabolic disorder, or neurodegenerative disorder.

3. The composition according to claim 1 or 2, wherein the therapy comprises repopulating mammalian bone marrow.

4. The composition according to any of claims 1 to 3, for use in the treatment of acute myelogeneous leukemia, acute lymphoblastic leukemia, chronic lymphocytic leukemia, chronic myelogeneous leukemia, non-Hodgkin lymphoma, severe aplastic anemia, severe combined immunodeficiency or sickle cell disease.

5. The composition according to claim 1, for use in gene therapy.

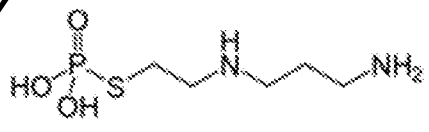
6. The composition of any preceding claim, wherein step i) comprises selecting for cells which are CD133+.

7. The composition of any preceding claim, wherein step i) comprises selecting for cells which are CD34+

8. The composition of any preceding claim, wherein the HDAC inhibitor is scriptaid or quisinostat.

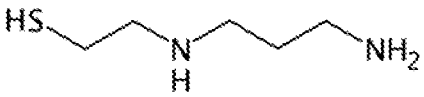
9. The composition of any preceding claim, wherein the HDAC inhibitor is scriptaid.

10. The composition of any preceding claim, wherein the aminothiol compound is amifostine:



or

WR1065:



11. The composition of any preceding claim, wherein the aminothiol compound is WR1065.

12. The composition of any preceding claim, wherein the isolated population is obtained from umbilical cord blood.

13. The composition of claims 1 to 12, wherein the isolated population is obtained from peripheral blood.

14. The composition of claims 1 to 12, wherein the isolated population obtained from bone marrow.

15. The composition of any of the preceding claims, wherein the steps ii) and iii) are carried out over a total time of 5 to 10 days to form expanded cells.

16. The composition of any preceding claim, wherein the cells are cultured in a serum free or feeder free tissue culture system.

17. The composition of any preceding claim, wherein the cells are obtained from a mammal, preferably a human.

18. The composition of any preceding claim, wherein the expanded cells are enriched for HSC.

19. The composition of any preceding claim, wherein the expanded cells are enriched for; Lin-, CD38-, CD34+, CD133+, CD45RA-, CD90+ and CD49f+.

20. The composition of any preceding claim, wherein the total cell expansion is between about 2-fold to about 20-fold.

21. The composition of any preceding claim, wherein the expansion of Lin-, CD38-, CD34+, CD133+, CD45RA-, CD90+ and CD49f+ cells is about 500-fold

22. The composition of any preceding claim, wherein the HDAC inhibitor is used at a concentration of 0.01-50 μM.

23. The composition of any preceding claim, wherein the aminothiol compound is used at a concentration of 50-500 μM.

24. A method of treatment comprising the steps of;

i) obtaining an isolated population of HSPC

ii) culturing the isolated population of HSPC in the presence of a histone deacetylase inhibitor (HDAC inhibitor), to form a cultured population

iii) adding an aminothiol compound having the formula $RNH(C_nH_{2n})NH(C_nH_{2n})SX$, wherein R is hydrogen, an aryl, an acyl, or an alkyl group containing from 1 to 7 carbon atoms, each n has a value of from 2 to 6 and X is H or PO_3H_2; or a pharmaceutically acceptable salt thereof, to the cultured population of HSPC to form expanded cells.

iv) administering the expanded cells to a subject.

25. The method of claim 23 comprising any of the additional features of claims 2 to 23.

26. Use of a composition comprising an expanded population of cells, in the manufacture of a medicament for use in therapy, wherein the cells have been expanded by the method comprising;

i) obtaining an isolated population of HSPC

ii) culturing the isolated population of HSPC in the presence of a histone deacetylase inhibitor (HDAC inhibitor), to form a cultured population

iii) adding an aminothiol compound having the formula $RNH(C_nH_{2n})NH(C_nH_{2n})SX$, wherein R is hydrogen, an aryl, an acyl, or an alkyl group containing from 1 to 7 carbon atoms, each n has a value of from 2 to 6 and X is H or PO_3H_2; or a pharmaceutically acceptable salt thereof, to the cultured population of HSPC to form expanded cells.

27. Use according to claim 26 comprising any of the additional features of claims 2 to 23.

CLAIMS

1. A composition comprising an expanded population of cells for use in therapy, in which the cells have been expanded by a method comprising:

(i) obtaining an isolated population of hematopoeitic stem and progenitor cells (HSPC);

(ii) culturing the isolated population of HSPC in the presence of a histone deacetylase inhibitor (HDAC inhibitor), to form a cultured population;

(iii) adding an aminothiol compound having the formula $RNH(C_nH_{2n})NH(C_nH_{2n})SX$, in which R is hydrogen, an aryl, an acyl, or an alkyl group containing from 1 to 7 carbon atoms, each n has a value of from 2 to 6 and X is H or PO_3H_2; or a pharmaceutically acceptable salt thereof, to the cultured population of HSPC to form expanded cells.

2. A composition for use according to Claim 1, in which the composition is for use in the treatment of a haematological disorder, immune disorder, metabolic disorder, or neurodegenerative disorder.

3. A composition for use according to Claim 1 or 2, in which the therapy comprises repopulating mammalian bone marrow.

4. A composition for use according to Claim 1, 2 or 3, in which the composition is for use in the treatment of acute myelogeneous leukemia, acute lymphoblastic leukemia, chronic lymphocytic leukemia, chronic myelogeneous leukemia, non-Hodgkin lymphoma, severe aplastic anaemia, severe combined immunodeficiency or sickle cell disease.

5. A composition for use according to Claim 1, in which the composition is for use in gene therapy.

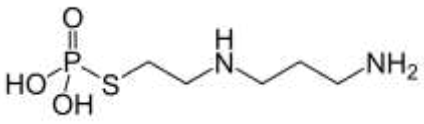
6. A composition for use according to any preceding claim, in which step (i) comprises selecting for cells which are CD133+.

7. A composition for use according to any preceding claim, in which step (i) comprises selecting for cells which are CD34+.

8. A composition for use according to any preceding claim, in which the HDAC inhibitor is scriptaid or quisinostat.

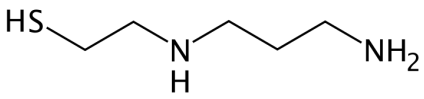
9. A composition for use according to any preceding claim, in which the HDAC inhibitor is scriptaid.

10. A composition for use according to any preceding claim, in which the aminothiol compound is amifostine:



or

WR1065:



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11. A composition for use according to any preceding claim, in which the aminothiol compound is WR1065.

12. A composition for use according to any preceding claim, in which the isolated population is obtained from umbilical cord blood.

13. A composition for use according to any preceding claim, in which the isolated population is obtained from peripheral blood.

14. A composition for use according to any of Claims 1 to 12, in which the isolated population obtained from bone marrow.

15. A composition for use according to any preceding claim, in which the steps (ii) and (iii) are carried out over a total time of 5 to 10 days to form expanded cells.

16. A composition for use according to any preceding claim, in which the cells are cultured in a serum free or feeder free tissue culture system.

17. A composition for use according to any preceding claim, in which the cells are obtained from a mammal, preferably a human.

18. A composition for use according to any preceding claim, in which the expanded cells are enriched for hematopoietic stem cells (HSC).

19. A composition for use according to any preceding claim, in which the expanded cells are enriched for; Lin-, CD38-, CD34+, CD133+, CD45RA-, CD90+ and CD49f+.

20. A composition for use according to any preceding claim, in which the total cell expansion is between 2-fold to 20-fold.

21. A composition for use according to any preceding claim, in which the expansion of Lin-, CD38-, CD34+, CD133+, CD45RA-, CD90+ and CD49f+ cells is about 500-fold.

22. A composition for use according to any preceding claim, in which the HDAC inhibitor is used at a concentration of 0.01-50 μM.

23. A composition for use according to any preceding claim, in which the aminothiol compound is used at a concentration of 50-500 μM.

24. Use of a composition comprising an expanded population of cells in the manufacture of a medicament for use in therapy, in which the cells have been expanded by a method comprising:

(i) obtaining an isolated population of HSPC;

(ii) culturing the isolated population of HSPC in the presence of a histone deacetylase inhibitor (HDAC inhibitor), to form a cultured population;

(iii) adding an aminothiol compound having the formula $RNH(C_nH_{2n})NH(C_nH_{2n})SX$, in which R is hydrogen, an aryl, an acyl, or an alkyl group containing from 1 to 7 carbon atoms, each n has a value of from 2 to 6 and X is H or PO_3H_2; or a pharmaceutically acceptable salt thereof, to the cultured population of HSPC to form expanded cells.

25. Use according to Claim 24 comprising any of the additional features of Claims 2 to 23.