Claims

1. A method to expand hematopoietic stem and progenitor cells (HSPC) wherein the method comprises:

i) obtaining an isolated population of HSPC;

ii) culturing the isolated population of HSPC for at least 48 hours to form a first cultured population;

iii) adding a histone deacetylase inhibitor (HDAC inhibitor) and further culturing the cells, to form a second cultured population; and

iv) adding an aminothiol compound to the second cultured population and further culturing the cells to form an expanded population of cells, wherein the aminothiol compound has 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.

2. 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 for at least 48 hours to form a first cultured population;

iii) adding a histone deacetylase inhibitor (HDAC inhibitor) and further culturing the cells, to form a second cultured population; and

iv) adding an aminothiol compound to the second cultured population and further culturing the cells to form an expanded population of cells, wherein the aminothiol compound has 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.

3. 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 for at least 48 hours to form a first cultured population;

iii) adding a histone deacetylase inhibitor (HDAC inhibitor) and further culturing the cells, to form a second cultured population; and

iv) adding an aminothiol compound to the second cultured population and further culturing the cells to form an expanded population of cells, wherein the aminothiol compound has 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.

4. The composition according to claim 2, or the use according to claim 3, wherein:

the therapy or treatment is of a haematological disorder, immune disorder, metabolic disorder, or neurodegenerative disorder; and/or

the therapy or treatment comprises repopulating mammalian bone marrow; and/or

the therapy or treatment is 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 2, or the use according to claim 3, wherein the therapy or treatment is gene therapy.

6. The method, composition, or use according to any of the preceding claims, wherein:

step i) comprises selecting for cells which are CD133+; and/or

step i) comprises selecting for cells which are CD34+; and/or

step ii) comprises culturing the cells for about 48 hours to about 96 hours, preferably about 72 hours; and/or

step iii) comprises culturing the cell for about 24 hours to about 72 hours, preferably about 48 to 72 hours; and/or

the cells in the first cultured population proliferate more than the cells in the second cultured population; and/or

step iv) comprises culturing the cell for about 16 hours to about 24 hours, preferably about 24 hours; and/or

step ii) comprises culturing the cell in the presence of basal media; and/or

step ii) further comprises culturing the cell in the presence of interleukin 6 (IL-6); and/or

step ii) comprises culturing the cell in the presence of nicotinamide, pyrimido-indole derivatives such as UM171 and UM729, p38 MAPK inhibitors, Notch ligands, Wnt agonists, a JNK inhibitor, a cytokine, at least one RET agonist and/or an antagonist of the aryl hydrocarbon receptor.

7. The method, composition, or use according to any of the preceding claims, wherein:

between step ii) and step iii) the cells are washed, preferably wherein the cell culture medium at stage iii) onwards is substantially free of the JNK inhibitor and/or the antagonists of the aryl hydrocarbon; and/or

the JNK inhibitor is SP600125; and/or

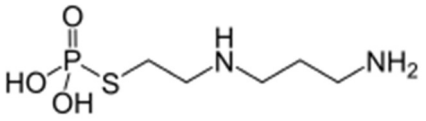
the antagonist of the aryl hydrocarbon receptor is SR1; and/or

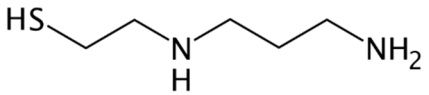
step ii) comprises culturing the cells in the presence of at least one, preferably at least two RET agonist(s); and/or

the at least one, preferably at least two RET agonist(s) is selected from GDNF, GFRα1, BT-13, Q525 and BT44, preferably wherein the RET agonist is selected from GDNF and GFRα1.

8. The method, composition, or use according to any of the preceding claims, wherein:

the HDAC inhibitor is scriptaid or quisinostat; and/or

the aminothiol compound is amifostine,  or

 WR1065, .

9. The method, composition, or use according to any of the preceding claims, wherein the isolated population is obtained from any one of umbilical cord blood, peripheral blood, or bone marrow.

10. The method, composition, or use according to any of the preceding claims, wherein:

the steps ii), iii) and iv) are carried out over a total time sufficient for the isolated population of HSPC to form expanded cells; and/or

the steps ii), iii) and iv) are carried out over a total time of about 3 to 8 days; and/or

the cells are cultured in a serum free or feeder free tissue culture system; and/or

the cells are obtained from a mammal, preferably a human.

11. The method, composition, or use according to any of the preceding claims, wherein:

the expanded cells are enriched for hematopoietic stem cells (HSC) and/or long-term hematopoietic stem cells (LT-HSC); and/or

the expanded cells are enriched for: Lin-, CD38-, CD34+, CD45RA-, CD90+, CD201+ and CD49f+; and/or

the total cell expansion is between about 5-fold to about 20-fold, preferably about 10-fold to about 20-fold; and/or

the expansion of Lin-, CD38-, CD34+, CD45RA-, CD90+ and CD49f+ cells is about 500-fold.

12. The method, composition, or use according to any of the preceding claims, wherein:

the JNK inhibitor is used at a concentration of 0.01-50 μM, preferably 0.2 μM; and/or

the antagonist aryl hydrocarbon receptor is used at a concentration of 0.01-50 μM, preferably 1 μM; and/or

the IL-6 is used at a concentration of 0.01-50 μg/ml, preferably 0.1 μg/ml; and/or

the at least one, preferably two RET agonist(s) is used at a concentration of 100 ng/ml; and/or

the HDAC inhibitor is used at a concentration of 0.01-50 μM, preferably 0.3 μM; and/or

the aminothiol compound is used at a concentration of 50-500 μM, preferably 100 μM.

13. A kit for the expansion of HSPC according to claim 1, wherein the kit comprises; sterile elements for the expansion of HSPC, a HDAC inhibitor and 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.

14. A kit according to claim 13, with any of the additional features of claims 6 to 12.

15. An expanded population of cells obtainable by the method according to any of claims 1 or 6 to 12.