

CLAIMS

What is claimed is:

1. A method of stem cell transplantation in a subject in need thereof comprising:
 - (a) expanding hematopoietic stem or progenitor cells (HSPCs) by contacting the HSPCs with endothelial cells (ECs) at an initial EC/HSPC ratio for a first time period under conditions allowing for expansion of the HSPCs, to produce an expanded cell population comprising HSPCs and ECs at an expanded HSPC/EC ratio; and
 - (b) transfusing the expanded cell population obtained from step (a) into the subject;wherein a continuous interaction is maintained between the HSPCs and the ECs throughout the expansion and the transfusion steps.
2. The method according to claim 1, wherein the HSPCs are hematopoietic stem cells.
3. The method according to claim 1, wherein the HSPCs are allogeneic with respect to the subject.
4. The method according to claim 3, wherein the HSPCs are umbilical cord blood HSPCs.
5. The method according to claim 1, wherein the HSPCs are autologous with respect to the subject.
6. The method according to claim 5, wherein the HSPCs are gene-modified steady state bone marrow derived HSPCs.
7. The method according to claim 1, wherein the ECs are vascular ECs.
8. The method according to claim 1, wherein the ECs are mitotically inactivated prior to the expansion.

9. The method according to claim 1, wherein the ECs are E4ORF1+ engineered ECs.
10. The method according to claims 1, wherein the ECs are E4ORF1+ ETV2+ engineered ECs.
11. The method according to claim 10, wherein the ECs are also E4ORF6+.
12. The method according to claim 10, wherein the ECs comprise a recombinant nucleic acid molecule that encodes an ETV2 polypeptide.
13. The method according to claim 10, wherein the ECs comprise a recombinant nucleic acid molecule that encodes an adenovirus E4ORF1 polypeptide.
14. The method according to claim 11, wherein the ECs comprise a recombinant nucleic acid molecule that encodes an adenovirus E4ORF6 polypeptide.
15. The method according to any one of claims 12 to 14, wherein the nucleic acid molecule is in the form of a plasmid vector.
16. The method according to any one of claims 12 to 14, wherein the nucleic acid molecule is integrated into the genomic DNA of the engineered ECs.
17. The method according to any one of claims 12 to 16, wherein the ECs are differentiated ECs.
18. The method according to any one of claims 12 to 16, wherein the ECs are adult ECs.
19. The method according to any one of claims 12 to 16, wherein the ECs are not embryonic ECs.
20. The method according to any one of claims 12 to 16, wherein the ECs are human ECs.

21. The method according to any one of claims 12 to 16, wherein the ECs are primary ECs.
22. The method according to any one of claims 12 to 16, wherein the ECs are human umbilical vein ECs (HUVECs).
23. The method according to claim 1, wherein the initial EC/HSPC ratio is at least about 200:1.
24. The method according to claim 1, wherein the first time period is about 1 day to about 24 days.
25. The method according to claim 1, wherein the expanded cell population comprises about 1.0×10^6 to about 1.0×10^8 HSPCs/kg subject.
26. The method according to claim 1, wherein the expanded HSPC/EC ratio is about 10:1 to about 1:10.
27. The method according to claim 1, wherein the continuous interaction between the HSPCs and the ECs comprises continuous contact between the HSPCs and the ECs during the expansion step, and continuous proximity of the HSPCs and the ECs during the expansion and transfusion steps combined.
28. The method according to claim 1, wherein the platelet count in the circulating blood of the subject is at least about 20,000/ μ L by about 15 days to about 35 days after transfusing the expanded cell population into the subject.
29. The method according to claim 1, wherein the absolute neutrophil count in the circulating blood of the subject is at least about 100/ μ L by about 5 days to about 20 days after transfusing the expanded cell population into the subject.

30. The method according to claim 1, wherein the absolute neutrophil count in the circulating blood of the subject is at least about 500/ μ L by about 10 days to about 25 days after transfusing the expanded cell population into the subject.
31. The method according to claim 1, wherein the absolute neutrophil count in the circulating blood of the subject is at least about 500/ μ L at about 1,000 days after transfusing the expanded cell population into the subject.
32. The method according to claim 1, wherein the subject has a deficiency in hematopoiesis caused by a myeloablative treatment, or a disorder selected from: a hematologic disease, a disorder that requires bone marrow hematopoietic stem cell transplantation, an infectious immunodeficiency, an infectious disease affecting T cells, HIV, a genetic immunodeficiency, severe combined immunodeficiency, a genetic disease affecting erythrocytes, an anemia, and Fanconi anemia.
33. The method according to claim 1, wherein the subject is human.
34. A composition comprising HSPCs and ECs for use in stem cell transplantation in a subject in need thereof, wherein the stem cell transplantation comprises the method according to claim 1.
35. The composition according to claim 34, wherein the HSPCs are hematopoietic stem cells.
36. The composition according to claim 34 or 35, wherein the HSPCs are allogeneic with respect to the subject.
37. The composition according to claim 36, wherein the HSPCs are umbilical cord blood HSPCs.
38. The composition according to claim 34 or 35, wherein the HSPCs are autologous with respect to the subject.

39. The composition according to claim 38, wherein the HSPCs are gene-modified steady state bone marrow derived HSPCs.
40. The composition according to claim 34, wherein the ECs are vascular ECs.
41. The composition according to claim 34, wherein the ECs are mitotically inactivated prior to the expansion.
42. The composition according to claim 34, wherein the ECs are E4ORF1+ engineered ECs.
43. The composition according to claim 34, wherein the ECs are E4ORF1+ ETV2+ engineered ECs.
44. The composition according to claim 43, wherein the ECs are also E4ORF6+.
45. The composition according to claim 43, wherein the ECs comprise a recombinant nucleic acid molecule that encodes an ETV2 polypeptide.
46. The composition according to claim 43, wherein the ECs comprise a recombinant nucleic acid molecule that encodes an adenovirus E4ORF1 polypeptide.
47. The composition according to claim 44, wherein the ECs comprise a recombinant nucleic acid molecule that encodes an adenovirus E4ORF6 polypeptide.
48. The composition according to claim 45, wherein the nucleic acid molecule is in the form of a plasmid vector.
49. The composition according to claim 45, wherein the nucleic acid molecule is integrated into the genomic DNA of the engineered ECs.
50. The composition according to claim 45, wherein the ECs are differentiated ECs.

51. The composition according to claim 45, wherein the ECs are adult ECs.
52. The composition according to claim 45, wherein the ECs are not embryonic ECs.
53. The composition according to claim 45, wherein the ECs are human ECs.
54. The composition according to claim 45, wherein the ECs are primary ECs.
55. The composition according to claim 45, wherein the ECs are human umbilical vein ECs (HUVECs).
56. The composition according to claim 34, wherein the initial EC/HSPC ratio is at least about 200:1.
57. The composition according to claim 34, wherein the first time period is about 1 day to about 24 days.
58. The composition according to claim 34, wherein the expanded cell population comprises about 1.0×10^6 to about 1.0×10^8 HSPC cells/kg subject.
59. The composition according to claim 34, wherein the expanded HSPC/EC ratio is about 10:1 to about 1:10.
60. The composition according to claim 34, wherein the continuous interaction between the HSPCs and the ECs comprises continuous contact between the HSPCs and the ECs during the expansion step, and continuous proximity of the HSPCs and the ECs during the expansion and transfusion steps combined.
61. The composition according to claim 34, wherein the platelet count in the circulating blood of the subject is at least about 20,000/ μ L by about 15 days to about 35 days after transfusing the expanded cell population into the subject.

62. The composition according to claim 34, wherein the absolute neutrophil count in the circulating blood of the subject is at least about 100/ μ L by about 5 days to about 20 days after transfusing the expanded cell population into the subject.
63. The composition according to claim 34, wherein the absolute neutrophil count in the circulating blood of the subject is at least about 500/ μ L by about 10 days to about 25 days after transfusing the expanded cell population into the subject.
64. The composition according to claim 34, wherein the absolute neutrophil count in the circulating blood of the subject is at least about 500/ μ L at about 1,000 days after transfusing the expanded cell population into the subject.
65. The composition according to claim 34, wherein the subject has a deficiency in hematopoiesis caused by a myeloablative treatment, or a disorder selected from: a hematologic disease, a disorder that requires bone marrow hematopoietic stem cell transplantation, an infectious immunodeficiency, an infectious disease affecting T cells, HIV, a genetic immunodeficiency, severe combined immunodeficiency, a genetic disease affecting erythrocytes, an anemia, and Fanconi anemia.
66. The composition according to claim 34, wherein the subject is human.