wherein a continuous interaction is maintained between the HSPCs and the ECs throughout the expansion and the transfusion steps.

A further aspect of the present invention relates to compositions comprising HSPCs and ECs for use in stem cell transplantation in a subject in need thereof, wherein the stem cell transplantation comprises the methods described herein. Preferably, the ECS are in continuous proximity with the HSPCs throughout the expansion and transfusion steps, as described and shown herein. Still more preferably, the ECs are in continuous contact with the HSPCs during at least the expansion step.

A further aspect of the present invention relates to a method of producing a mixed population of hematopoietic stem or progenitor cells (HSPCs) and endothelial cells (ECs) for use in stem cell transplantation in a subject in need thereof, the method comprising: (1) contacting HSPCs with endothelial cells (ECs) at an initial EC/HSPC ratio, (2) culturing the HSPCs and ECs 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 (3) subsequently harvesting the entirety of the cellular material from the culturing step; wherein (a) the HSPCs and the ECs are simultaneously present in the same medium throughout the culturing process and (b) at no point during the culturing process are the HSPCs removed from the ECs or contacted with additional ECs, and (c) there is no purification step to separate the ECs from the HSPCs, such that a continuous interaction is maintained between the HSPCs and the ECs throughout the expansion and the harvesting steps, thereby producing a mixed population of hematopoietic stem or progenitor cells (HSPCs) and endothelial cells (ECs) for use in stem cell transplantation.

A further aspect of the present invention relates to a composition comprising HSPCs and ECs for use in stem cell transplantation in a subject in need thereof, wherein the composition is produced using the method as described herein.

In some embodiments, the initial EC/HSPC ratio is at least about 200:1. In some embodiments, the initial EC/HSPC ratio is at least about 300:1. In some embodiments, the initial EC/HSPC ratio is at least about 400:1. In some embodiments, the initial EC/HSPC ratio is at least about 500:1. In some embodiments, the initial EC/HSPC ratio is at least about 600:1. In some embodiments, the initial EC/HSPC ratio is at least about 700:1. In some embodiments, the initial EC/HSPC ratio is at least about 1000:1. In some embodiments, the initial EC/HSPC ratio

is at least about 2000:1. In some embodiments, the initial EC/HSPC ratio is at least about 3000:1.

In some embodiments, the expanded HSPC/EC ratio is about 10:1 to about 1:10. In some embodiments, the expanded HSPC/EC ratio is about 10:1 to about 1:1. In some embodiments, the expanded HSPC/EC ratio is about 9:1 to about 2:1. In some embodiments, the expanded HSPC/EC ratio is about 8:1 to about 3:1. In some embodiments, the expanded HSPC/EC ratio is about 7:1 to about 4:1. In some embodiments, the expanded HSPC/EC ratio is about 6:1 to about 5:1.

A further aspect of the present invention relates to kits or systems for isolating, expanding, preserving and administering HSPCs and endothelial cells in accordance with the methods described herein.

BRIEF DESCRIPTION OF THE DRAWINGS

The skilled artisan will understand that the drawings are for illustration purposes only, and are not intended to limit the scope of the present teachings in any way.

Figure 1 shows phase microscopy images of the effect of radiation exposure on E4ORF1+ engineered ECs. ECs were harvested under standard culture conditions and

CLAIMS

What is claimed is:

1. A method of producing a mixed population of hematopoietic stem or progenitor cells (HSPCs) and endothelial cells (ECs) for use in stem cell transplantation in a subject in need thereof, the method comprising: (1) contacting HSPCs with endothelial cells (ECs) at an initial EC/HSPC ratio, (2) culturing the HSPCs and ECs 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 (3) subsequently harvesting the entirety of the cellular material from the culturing step; wherein (a) the HSPCs and the ECs are simultaneously present in the same medium throughout the culturing process and (b) at no point during the culturing process are the HSPCs removed from the ECs or contacted with additional ECs, and (c) there is no purification step to separate the ECs from the HSPCs, such that a continuous interaction is maintained between the HSPCs and the ECs throughout the expansion and the harvesting steps, thereby producing a mixed population of hematopoietic stem or progenitor cells (HSPCs) and endothelial cells (ECs) for use in stem cell transplantation.

2. The method according to claim 1, wherein the HSPCs are allogeneic with respect to the subject.

3. The method according to claim 2, wherein the HSPCs are umbilical cord blood HSPCs.

4. The method according to claim 1, wherein the HSPCs are autologous with respect to the subject.

5. The method according to claim 1, wherein the ECs are E4ORF1+ engineered ECs.

6. The method according to claims 1, wherein the ECs are E4ORF1+ ETV2+ engineered ECs.

7. The method according to claim 1, wherein the ECs are primary ECs.

8. The method according to claim 1, wherein the ECs are human umbilical vein ECs (HUVECs).

9. The method according to claim 1, wherein the initial EC/HSPC ratio is at least about 200:1.

10. The method according to claim 1, wherein the first time period is about 1 day to about 24 days.

11. 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.

12. A composition comprising HSPCs and ECs for use in stem cell transplantation in a subject in need thereof, wherein the composition is produced using the method according to claim 1.

13. The composition according to claim 12, wherein the ECs are E4ORF1+ engineered ECs.

14. The composition according to claim 12, wherein the ECs are E4ORF1+ ETV2+ engineered ECs.

15. The composition according to claim 12, 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.

16. The method of claim 1, wherein the initial EC/HSPC ratio is at least about 100:1.