CLAIMS

1. A pharmaceutical composition comprising bone marrow tissue, hematopoietic cells, differentiated blood cells, or bone marrow-derived factors obtained from a bone marrow tissue maintained *ex vivo* by:

implanting an implantation device in a subject whereby the implantation device is colonized after implantation by at least one of stem cells, vascular cells, immune cells, differentiated cells and diseased cells;

removing the implantation device and the tissue contained in the implantation device from the subject; and

providing a perfusion fluid to the tissue.

2. A composition according to Claim 1, in which the bone marrow tissue and/or hematopoietic cells are contained within an implantation device.

3. A pharmaceutical composition comprising bone marrow tissue, hematopoietic cells, differentiated blood cells, or bone marrow-derived factors obtained from a bone marrow tissue maintained *ex vivo* by:

implanting an implantation device in a subject whereby the implantation device is colonized after implantation by at least one of stem cells, vascular cells, immune cells, differentiated cells and diseased cells;

removing the implantation device and the tissue contained in the implantation device from the subject;

removing the tissue from the implantation device; and

providing a perfusion fluid to the tissue.

4. A composition according to any of Claims 1, 2 or 3, in which the implantation device includes at least one cell growth chamber and at least one open port providing a passage to the cell growth chamber to enable cells to enter the cell growth chamber for cell colonization.

5. A composition according to any preceding claim, in which the tissue is placed in a microfluidic system prior to providing perfusion fluid.

6. A pharmaceutical composition comprising bone marrow tissue, hematopoietic cells, differentiated blood cells, or bone marrow-derived factors obtained from a bone marrow tissue maintained *ex vivo* by:

implanting a microfluidic implantation device in a subject whereby the microfluidic implantation device is colonized after implantation by at least one of stem cells, vascular cells, immune cells, differentiated cells and diseased cells;

removing the microfluidic implantation device and the tissue contained in the microfluidic implantation device from the subject; and

providing a perfusion fluid to the tissue.

7. A composition according to 6, in which the microfluidic device is connected to a microfluidic system after removal from the subject.

8. A composition according to any of Claims 6 or 7, in which the microfluidic device includes at least one cell growth chamber and at least one open port providing a passage to the cell growth chamber to enable cells to enter the cell growth chamber for cell colonization.

9. A composition according to any of Claims 6, 7 or 8, in which the microfluidic device includes at least one fluid channel separated from the at least one cell growth chamber by a porous separation component.

10. A composition according to any of Claims 6 to 9, in which the microfluidic device includes at least one inlet port and at least one outlet connecting the at least one fluid channel to the microfluidic system and providing perfusion fluid to the at least one cell growth chamber through the porous separation component.

11. A composition according to any preceding claim, in which the implantation device is implanted such that at least one port faces the muscle tissue of the subject.

12. A composition according to any preceding claim, in which the hematopoietic cells are selected from the group consisting of red blood cells, white blood cells, platelets, hematopoietic stem cells, lymphocytes, eosinophils, neutrophils, monocytes, hematopoietic progenitor cells, stromal cells, and a mixture of two or more of these cell types.

13. A composition according to any preceding claim, in which the bone marrow-derived factors are selected from the group consisting of a peptide, protein, small molecule, nucleotides, lipids, carbohydrates, cytokines and growth factors.

14. A composition according to any preceding claim, in which the subject is a non-human subject.

15. A composition according to any preceding claim, in which the subject is a non-human subject having human or humanized hematopoietic cells.

16. A composition according to Claim 15, in which the non-human subject has human hematopoietic cells obtained from a cancer or a human having a hematopoietic disease.

17. A composition according to Claim 16, in which the cancer is selected from the group consisting of leukemia, lymphoma, Hodgkin's lymphoma, myeloproliferative disorders, Langerhans cell histiocytosis, myeloma, and myelodysplastic syndromes.

18. A composition according to Claim 16, in which the hematopoietic disease is selected from the group consisting of thalassemia, factor IX deficiency, hemophilia, sickle cell disease, amyloidosis, agranulocytosis, anemia, leucopenia, neutropenia, thrombocytopenia, panctyopenia, Glanzmann's thrombasthenia, uremia, platelet storage pool disease, Von Willebrand disease, and afibrinogenemia.

19. A composition according to any preceding claim, in which the tissue or cells are maintained *ex vivo* at any stage of development.

20. A composition according to any preceding claim, in which the tissue or cells are genetically modified after removing the implantation device from the subject.

21. A composition according to any preceding claim for use in a method of therapy, the method comprising administering the hematopoietic cells and/or bone marrow-derived factors to a second subject.

22. A composition according to Claim 21 for a use as specified therein, in which the second subject has a condition selected from the group consisting of a compromised immune system, a cancer, an auto-immune disease, radiation toxicity, and a hematopoietic disease.

23. A composition according to Claim 22 for a use as specified therein, in which the cancer is selected from the group consisting of leukemia, lymphoma, Hodgkin's lymphoma, myeloproliferative disorders, Langerhans cell histiocytosis, myeloma, and myelodysplastic syndromes.

24. A composition according to Claim 22 for a use as specified therein, in which the hematopoietic disease is selected from the group consisting of thalassemia, factor IX deficiency, hemophilia, sickle cell disease, amyloidosis, agranulocytosis, anemia, leucopenia, neutropenia, thrombocytopenia, panctyopenia, Glanzmann's thrombasthenia, uremia, platelet storage pool disease, Von Willebrand disease, and afibrinogenemia.

25. A composition according to any of Claims 21 to 24 for a use as specified therein, in which the second subject has undergone chemotherapy and/or radiation therapy.

26. A composition according to any of Claims 21 to 25 for a use as specified therein, in which the first and second subjects are the same individual and the use further comprises an additional step of maintaining either the implantation device containing bone marrow tissue and/or hematopoietic cells or the bone marrow tissue or hematopoietic cells after removal from the implantation device between removal from the site of implantation and transplantation into the subject.

27. A composition according to any of Claims 21 to 26 for a use as specified therein, in which the use comprises an additional step of maintaining either the implantation device containing bone marrow tissue and/or hematopoietic cells or the bone marrow tissue or hematopoietic cells after removal from the implantation device between removal from the site of implantation and transplantation into the second subject.

28. A composition according to any of Claims 21 to 27 for a use as specified therein, in which maintaining the implantation device containing bone marrow tissue or hematopoietic cells *ex vivo* comprises freezing or refrigerating either the implantation device containing bone marrow tissue and/or hematopoietic cells or the bone marrow tissue and/or hematopoietic cells after removal from the implantation device.

29. A composition according to any of Claims 21 to 28 for a use as specified therein, in which maintaining the implantation device containing bone marrow tissue or hematopoietic

cells *ex vivo* comprises: connecting the implantation device to a microfluidic systems; and providing a perfusion fluid to the implantation device.

CLAIMS

1. A method of culturing human cells, the method comprising:

providing a device colonized by bone marrow tissue and having a partially or completely decellularised architecture;

treating the bone marrow tissue to retain the architecture;

introducing human hematopoietic stem cells into the architecture; and

providing a perfusion fluid to maintain the human hematopoietic stem cells *ex vivo*.

2. A method according to Claim 1, further comprising the step of removing the bone marrow tissue from the implantation device prior to providing perfusion fluid, and optionally further comprising the step of placing the bone marrow tissue in a microfluidic system prior to providing perfusion fluid.

3. A method according to Claim 1 or 2, in which the implantation device is a microfluidic device, and in which the method optionally further comprises connecting the microfluidic device to a microfluidic system; and/or

in which the microfluidic device includes at least one cell growth chamber and at least one open port providing a passage to the cell growth chamber to enable bone marrow tissue to enter the cell growth chamber for colonization; and/or

in which the microfluidic device includes at least one fluid channel separated from the at least one cell growth chamber by a porous separation component; and/or

in which the microfluidic device includes at least one inlet port and at least one outlet connecting the at least one fluid channel to the microfluidic system and providing perfusion fluid to the at least one cell growth chamber through the porous separation component.

4. A method according to Claim 1, 2 or 3, in which the hematopoietic cells are selected from the group consisting of red blood cells, white blood cells, platelets, hematopoietic stem cells, lymphocytes, eosinophils, neutrophils, monocytes, hematopoietic progenitor cells, stromal cells, and a mixture of two or more of these cell types.

5. A method according to Claim 4, in which the hematopoietic cells are suitable for administration to a subject,

in which the subject optionally has a condition selected from the group consisting of a compromised immune system, a cancer, an auto-immune disease, radiation toxicity, and a hematopoietic disease,

in which the cancer is optionally selected from the group consisting of leukemia, lymphoma, Hodgkin's lymphoma, myeloproliferative disorders, Langerhans cell histiocytosis, myeloma, and myelodysplastic syndromes,

in which the hematopoietic disease is optionally selected from the group consisting of thalassemia, factor IX deficiency, hemophilia, sickle cell disease, amyloidosis, agranulocytosis, anemia, leucopenia, neutropenia, thrombocytopenia, panctyopenia, Glanzmann's thrombasthenia, uremia, platelet storage pool disease, Von Willebrand disease, and afibrinogenemia,

in which the subject has optionally undergone chemotherapy and/or radiation therapy.

6. A method according to any preceding claim, in which the hematopoietic cells maintained *ex vivo* are used to test the effect of compounds on the cells or interaction of compounds with the cells, where the compound is selected from the group consisting of chemotherapeutics, radiation therapies, modifiers of differentiation, formation, function or remodeling, hormones, nucleic acids, peptides, proteins, antibodies, small molecules, drug leads, enzymes, cells, viruses, bacteria, parasites, nucleotides, markers, dyes, imaging agents, enzymes, nanoparticles, and gene silencing molecules.

7. A method according to any preceding claim, in which the implantation device is suitable for implantation into a non-human subject; and/or

in which the implantation device is suitable for implantation into a non-human subject having human or humanized hematopoietic cells; and/or

in which the non-human subject has human hematopoietic cells obtained from a cancer or a human having a hematopoietic disease; and/or

in which the cancer is selected from the group consisting of leukemia, lymphoma, Hodgkin's lymphoma, myeloproliferative disorders, Langerhans cell histiocytosis, myeloma, and myelodysplastic syndromes; and/or

in which the hematopoietic disease is selected from the group consisting of thalassemia, factor IX deficiency, hemophilia, sickle cell disease, amyloidosis, agranulocytosis,

anemia, leucopenia, neutropenia, thrombocytopenia, panctyopenia, Glanzmann' s thrombasthenia, uremia, platelet storage pool disease, Von Willebrand disease, and afibrinogenemia.

8. A method of culturing human cells for implantation into a subject, the method comprising: providing a device colonized by bone marrow tissue from a first subject and having a partially or completely decellularised architecture;

treating the bone marrow tissue to retain the architecture;

introducing human hematopoietic stem cells into the architecture and in which the device is suitable for implantation into a second subject thereby providing bone marrow tissue or cells to the second subject.

9. A method according to Claim 8, in which the device is a microfluidic device; and/or

in which the microfluidic device includes at least one cell growth chamber and at least one open port providing a passage to the cell growth chamber to enable cells to enter the cell growth chamber for cell colonization; and/or

in which the microfluidic device includes at least one fluid channel separated from the at least one cell growth chamber by a porous separation component; and/or

in which the microfluidic device includes at least one inlet port and at least one outlet connecting the at least one fluid channel to the microfluidic system and providing perfusion fluid to the at least one growth channel through the porous separation component.

10. A method according to Claim 8 or 9, in which the tissue or cells comprise bone marrow tissue or hematopoietic cells.

11. A method according to Claim 8, 9 or 10, in which the second subject has been diagnosed with a condition selected from the group consisting of a compromised immune system, a cancer, an auto-immune disease, and a hematopoietic disease; and/or has undergone chemotherapy and/or radiation therapy; and/or

in which the cancer is selected from a group consisting of leukemia, lymphoma, Hodgkin's lymphoma, myeloproliferative disorders, Langerhans cell histiocytosis, myeloma, and myelodysplastic syndromes; and/or

in which the hematopoietic disease is selected from the group consisting of thalassemia, factor IX deficiency, hemophilia, sickle cell disease, amyloidosis, agranulocytosis, anemia, leucopenia, neutropenia, thrombocytopenia, panctyopenia, Glanzmann' s thrombasthenia, uremia, platelet storage pool disease, Von Willebrand disease, and afibrinogenemia; and/or in which the device is provided from a non-human first subject having human or humanized hematopoietic cells; and/or

in which the first and second subjects are the same individual and the method comprises an additional step of maintaining the device containing bone marrow tissue and/or hematopoietic cells; and/or

in which maintaining the device containing bone marrow tissue or hematopoietic cells *ex vivo* comprises freezing or refrigerating either the device containing bone marrow tissue and/or hematopoietic cells; and/or

in which maintaining the device containing bone marrow tissue or hematopoietic cells *ex vivo* comprises connecting the device to a microfluidic system, and

providing a perfusion fluid to the device; and/or

in which the tissue or cells contained within the device are genetically modified before implantation into the second subject.

12. A method for producing or manufacturing hematopoietic cells, the method comprising providing a device colonized by bone marrow tissue and having a partially or completely decellularised architecture; treating the bone marrow tissue to retain the architecture; introducing human hematopoietic stem cells into the architecture; providing a perfusion fluid to the tissue to maintain the human hematopoietic stem cells *ex vivo*; in which the device includes at least one cell growth chamber and at least one open port providing a passage to the cell growth chamber to enable cells to enter the cell growth chamber for cell colonization; and in which the hematopoietic cells are optionally selected from the group consisting of red blood cells, white blood cells, platelets, hematopoietic stem cells, lymphocytes, eosinophils, neutrophils, monocytes, a hematopoietic progenitor cell, and a mixture of two or more of these cell types.