CLAIMS

1. A method of preparing cells for therapeutic use, the method comprising culturing a population of progenitor cells in cell culture conditions that promote differentiation of the progenitor cells comprising the presence of: G-CSF, GM-CSF, IL-3 and TNF; to produce a population of granulopoietic cells.

2. The method according to claim 1, wherein the cell culture conditions that promote differentiation of the progenitor cells further comprise at least one supplement from the group consisting of: SCF; TPO; ITS; and HSA, optionally wherein the cell culture condition that promote differentiation of the progenitor cells comprise:

(i) GM-CSF at a concentration of approximately 0.01µg/mL; and
(ii) G-CSF at a concentration of approximately 0.13µg/mL; and
(iii) SCF at a concentration of approximately 0.13µg/mL; and
(iv) TPO at a concentration of approximately 0.13µg/mL; and
(v) IL-3 at a concentration of approximately 0.13µg/mL; and
(vi) TNF at a concentration of approximately 0.001µg/mL; and
(vii) ITS; and
(viii) HSA at approximately 1%.

3. The method according to claim 1 or 2, wherein the progenitor cells are cultured for 4 to 6 days in conditions to produce a population of granulopoietic cells, optionally wherein the progenitor cells are cultured for 4 or 5 days in conditions to produce a population of granulopoietic cells.

4. The method according to any preceding claim, wherein GM-CSF and IL-3 are provided to the cells for the final 48 hours of the period for which they are in culture, and/or wherein TNF is provided to the cells for the final 24 hours of the period for which they are in culture, and/or further comprising a step of culturing a population of stem cells (preferably haematopoietic stem cells [HSCs]) in cell culture conditions to produce the population of progenitor cells:

wherein the cell culture conditions for producing the progenitor cells comprise the presence of

(a) SCF,
(b) Flt-3 Ligand,
(c) IL-3,
(d) IL-6, and

(e) TPO.

5. The method according to claim 4, wherein the cell culture conditions for producing the progenitor cells comprise:

(i) SCF at a concentration of approximately 0.2µg/mL; and
(ii) Flt-3 Ligand at a concentration of approximately 0.2µg/mL; and
(iii) IL-3 at a concentration of approximately 0.015µg/mL; and
(iv) IL-6 at a concentration of approximately 0.015µg/mL; and
(v) TPO at a concentration of approximately 0.02µg/mL; and
(vi) ITS; and
(vii) HSA at approximately 1%.

6. The method according to claim 4 or 5, wherein the stem cells are cultured for 8-9 days in conditions to produce a population of progenitor cells, optionally wherein the stem cells are cultured for 8 days in conditions to produce a population of progenitor cells.

7. The method according to any preceding claim, further comprising a step of purifying the population of granulopoietic cells produced, and/or formulating the population of granulopoietic cells produced for medical use.

8. The method according to any preceding claim, further comprising priming the granulopoietic cells for therapeutic use, by a method comprising culturing the population of granulopoietic cells in the presence of GM-CSF, and optionally one or more cytokines selected from the group consisting of: TNF, IFN-α, IFN-β, IL-15, and IL-18, and optionally further comprising a step of purifying the population of primed granulopoietic cells produced, and/or formulating this population of cells for medical use.

9. A population of granulopoietic cells prepared for therapeutic use by a method of any of claims 1 to 8.

10. A granulopoietic cell or a population thereof, wherein the granulopoietic cell is:

(i) a CD64+ granulopoietic cell;
(ii) a CD16- granulopoietic cell; or
(iii) a CD62L- granulopoietic cell.

11. The granulopoietic cell or population thereof, according to claim 10(i), wherein the granulopoietic cell is:

CD64+ and CD16-;
CD64+ and CD62L-; and/or
CD64+, CD16- and CD62L-.

12. The granulopoietic cell or population thereof according to claim 10(ii), wherein the granulopoietic cell is CD16- and CD62L-.

13. An isolated population of granulopoietic cells comprising:

(i) a subpopulation of cells that are CD15+ CD64+ CD18+ CD49d+ CD71+; a subpopulation of cells that are CD15- CD11b+/- CD18+ CD49d+ CD32+ HLA-DR-; a subpopulation of cells that are CD15- CD11b- HLA-DR+ CD18+ CD49d+ and CD71+; and/or a subpopulation of cells that are CD15- CD11b+ HLA-DR+; or

(ii) more than 90% Lin- cells (for example, approximately 97% Lin- cells); less than 30% CD34+ cells (for example, approximately 14% CD34+ cells); more than 30% CD38+ cells (for example, approximately 65% CD38+ cells); less than 1% cells with an HSC phenotype (for example approximately 0.04% cells with an HSC phenotype); less than 1% cells with an LT-HSC phenotype (for example approximately 0.02% cells with an LT-HSC phenotype; less than 20% cells with an LMPP phenotype (for example approximately 5% cells with an LMPP phenotype); and less than 10% cells with an MPP phenotype (for example approximately 2.5% cells with an MPP phenotype).

14. The population of granulopoietic cells according to claim 13, wherein the subpopulation of cells that are CD15+ CD64+ CD18+ CD49d+ CD71+ and/or the subpopulation of cells that are CD15- CD11b+/- CD18+ CD49d+ CD32+ HLA-DR- are also positive for one, more than one, or all of the markers selected from the group consisting of: CD177, CD11b, CD71, CD66b, HLA-DR, CD115, CD49d, CD40, CD62L, CD54, CD18, CD34, CXCR4, CD64, CD32, CXCR2, CD38, Mac1, 4-1BBL, OX40L, PD-L1, and CD14, and/or wherein the subpopulation of cells that are CD15- CD11b- HLA-DR+ CD18+ CD49d+ and CD71+ are also positive for one, more than one, or all of the markers selected from the group consisting of: CD177, CD71, CD66b, CD115, CD49d, CD40, CD62L, CD54, CD18, CD34, CXCR4, CD64, CD32, CXCR2, CD38, Mac1, 4-1BBL, OX40L, PD-L1, and CD14.

15. A pharmaceutical composition comprising the population of granulopoietic cells according to any of claims 9 or 13-14 or the granulopoietic cell or the population thereof according to any of claims 10-12.

16. The population of granulopoietic cells according to any of claims 9 or 13-14, the granulopoietic cell or the population thereof according to any of claims 10-12, or the pharmaceutical composition according to claim 15, for use as a medicament.

17. Use of the population of granulopoietic cells according to any of claims 9 or 13-14, the granulopoietic cell or the population thereof according to any of claims 10-12, or the pharmaceutical composition according to claim 15, in the manufacture of a medicament for:

(i) treating cancer in a subject;

(ii) treating an infection in a subject; or

(iii) modulating a non-granulocytic therapeutic immune response.

18. The use according to claim 17(i), wherein the cancer is one or more of: pancreatic cancer, liver cancer, oesophageal cancer, stomach cancer, cervical cancer, ovarian cancer, lung cancer, bladder cancer, kidney cancer, brain cancer, prostate cancer, myeloma cancer, non-Hodgkin’s lymphoma (NHL), larynx cancer, uterine cancer, and breast cancer.

19. The use according to claim 17(iii), wherein the modulating is promoting.

20. A kit comprising:

(a) the population of granulopoietic cells according to any of claims 9 or 13-14;

(b) the granulopoietic cell or the population thereof according to any of claims 10-12; or

(c) the pharmaceutical composition according to claim 15; and

(d) optionally instructions for the use of the same (e.g. in treating cancer).