Claims

The invention claimed is:

1. A method of differentiating primate pluripotent stem cells into immature dendritic cells comprising contacting the primate pluripotent stem cells with a plurality of exogenous cytokines comprising granulocyte-macrophage colony stimulating factor (GM-CSF) and bone morphogenic protein 4 (BMP-4).

2. The method of claim 1, further comprising contacting the primate pluripotent stem cells with one or more of the following: vascular endothelial growth factor (VEGF), stem cell factor (SCF), fetal liver kinase ligand (FLT3L), thrombopoietin (TPO), interleukin 4 (IL-4) and interleukin 3 (IL-3).

3. The method of claim 1, wherein the primate pluripotent stem cells are human embryonic stem cells.

4. The method of claim 1, wherein the differentiation of the primate pluripotent stem cells into immature dendritic cells is performed under serum free conditions.

5. The method of claim 1, wherein the culture of the primate pluripotent stem cells and the differentiation of the primate pluripotent stem cells into immature dendritic cells is performed feeder free.

6. The method of claim 1, wherein the differentiation of the primate pluripotent stem cells into immature dendritic cells is performed stromal cell free.

7. The method of claim 1, further comprising making mature dendritic cells by contacting the immature dendritic cells with a maturation cocktail.

8. The method of claim 7, wherein the maturation cocktail comprises one or more of the following: tumor necrosis factor α (TNFα), interleukin 1β (IL1β), interferon γ (IFNγ), prostaglandin E2 (PGE2), polyinosinic: polycytidylic acid (POLY I:C), interferon α (IFNα), CD40 ligand (CD40L) and granulocyte macrophage colony stimulating factor (GM-CSF).

9. The method of claim 7, further comprising contacting the mature dendritic cell with an antigen.

10. The method of claim 9, wherein the antigen is a nucleic acid molecule expressing an antigen.

11. The method of claim 10, wherein the nucleic acid molecule is an RNA molecule expressing an antigen.

12. The method of claim 9, wherein the antigen is a peptide.

13. The method of claim 9 further comprising contacting the mature dendritic cell with a radiation source.

14. A method of differentiating primate pluripotent stem cells into immature dendritic cells comprising:

a) forming an embryoid body from the primate pluripotent stem cells;

b) contacting the embryoid body from a) with bone morphogenic protein 4 (BMP-4), vascular endothelial growth factor (VEGF) and stem cell factor (SCF) to differentiate the primate pluripotent stem cells into mesoderm;

c) contacting the mesoderm of b) with vascular endothelial growth factor (VEGF), stem cell factor (SCF), and GM-CSF to differentiate the mesoderm into hematopoietic stem cells;

d) contacting the hematopoietic stem cells of c) with SCF and granulocyte macrophage colony stimulating factor (GM-CSF) to differentiate the hematopoietic stem cells into monocytes; and

e) contacting the monocytes ofd) with granulocyte macrophage colony stimulating factor (GM-CSF) and interleukin 4 (IL-4) to differentiate the monocytes into immature dendritic cells.

15. A method of differentiating in vitro a cell expressing stage specific embryonic antigen 3 (SSEA3), stage specific embryonic antigen 4 (SSEA4) and markers detectable using antibodies designated Tra-1-60, and Tra-1-81 into a cell expressing CD11c comprising contacting the cell expressing stage specific embryonic antigen 3 (SSEA3), stage specific embryonic antigen 4 (SSEA4) and markers detectable using antibodies designated Tra-1-60, and Tra-1-81 with a differentiation cocktail comprising: GM-CSF and BMP-4.

16. The method of claim 15, further comprising contacting the cell expressing stage specific embryonic antigen 3 (SSEA3), stage specific embryonic antigen 4 (SSEA4) and markers detectable using antibodies designated Tra-1-60, and Tra-1-81 with VEGF.

17. The method of claim 15, further comprising contacting the cell expressing stage specific embryonic antigen 3 (SSEA3), stage specific embryonic antigen 4 (SSEA4) and markers detectable using antibodies designated Tra-1-60, and Tra-1-81 with SCF.

18. A system for the production of mitotically inactive antigen presenting cells comprising a) a first isolated cell population comprising pPS cells and b) a second isolated cell population comprising mitotically inactivated mature dendritic cells which are the in vitro progeny of a portion of the first isolated cell population.

19. The system of claim 18, wherein at least 5% of the mature dendritic cells express one or more markers chosen from CD86 and CD83.

20. The system of claim 19, wherein the mature dendritic cells expressing one or more markers chosen from CD86 and CD83 further express one or more of the following MHCII and CCR7.

21. The system of claim 18, wherein the first and second cell populations are both stromal cell free and free of exogenous IL-3.

22. The system of claim 18, wherein pPS cells are human embryonic stem cells.

23. The system of claim 18, wherein the mature dendritic cells are mitotically inactivated with radiation.

24. The system of claim 23, wherein the mature dendritic cells stimulate T cells to secrete interferon.

25. The system of claim 23, wherein the mature dendritic cells migrate in the presence of a chemotactic ligand.

The invention claimed is:

1. A method of differentiating primate pluripotent stem cells into immature dendritic cells comprising contacting the primate pluripotent stem cells with a plurality of exogenous cytokines comprising granulocyte-macrophage colony stimulating factor (GM-CSF) and bone morphogenic protein 4 (BMP-4).

2. The method of claim 1, further comprising contacting the primate pluripotent stem cells with one or more of the following: vascular endothelial growth factor (VEGF), stem cell factor (SCF), fetal liver kinase ligand (FLT3L), thrombopoietin (TPO), interleukin 4 (IL-4) and interleukin 3 (IL-3).

3. The method of claim 1, wherein the primate pluripotent stem cells are human embryonic stem cells.

4. The method of claim 1, wherein the differentiation of the primate pluripotent stem cells into immature dendritic cells is performed under serum free conditions.

5. The method of claim 1, wherein the culture of the primate pluripotent stem cells and the differentiation of the primate pluripotent stem cells into immature dendritic cells is performed feeder free.

6. The method of claim 1, wherein the differentiation of the primate pluripotent stem cells into immature dendritic cells is performed stromal cell free.

7. The method of claim 1, further comprising making mature dendritic cells by contacting the immature dendritic cells with a maturation cocktail.

8. The method of claim 7, wherein the maturation cocktail comprises one or more of the following: tumor necrosis factor α (TNFα), interleukin 1β (IL1β), interferon γ (IFNγ), prostaglandin E2 (PGE2), polyinosinic: polycytidylic acid (POLY I:C), interferon α (IFNα), CD40 ligand (CD40L) and granulocyte macrophage colony stimulating factor (GM-CSF).

9. The method of claim 7, further comprising contacting the mature dendritic cell with an antigen.

10. The method of claim 9, wherein the antigen is a nucleic acid molecule expressing an antigen.

11. The method of claim 10, wherein the nucleic acid molecule is an RNA molecule expressing an antigen.

12. The method of claim 9, wherein the antigen is a peptide.

13. The method of claim 9 further comprising contacting the mature dendritic cell with a radiation source.

14. A method of differentiating primate pluripotent stem cells into immature dendritic cells comprising:

a) forming an embryoid body from the primate pluripotent stem cells;

b) contacting the embryoid body from a) with bone morphogenic protein 4 (BMP-4), vascular endothelial growth factor (VEGF) and stem cell factor (SCF) to differentiate the primate pluripotent stem cells into mesoderm;

c) contacting the mesoderm of b) with vascular endothelial growth factor (VEGF), stem cell factor (SCF), and GM-CSF to differentiate the mesoderm into hematopoietic stem cells;

d) contacting the hematopoietic stem cells of c) with SCF and granulocyte macrophage colony stimulating factor (GM-CSF) to differentiate the hematopoietic stem cells into monocytes; and

e) contacting the monocytes of d) with granulocyte macrophage colony stimulating factor (GM-CSF) and interleukin 4 (IL-4) to differentiate the monocytes into immature dendritic cells.

15. A method of differentiating in vitro a cell expressing stage specific embryonic antigen 3 (SSEA3), stage specific embryonic antigen 4 (SSEA4) and markers detectable using antibodies designated Tra-1-60, and Tra-1-81 into a cell expressing CD11c comprising contacting the cell expressing stage specific embryonic antigen 3 (SSEA3), stage specific embryonic antigen 4 (SSEA4) and markers detectable using antibodies designated Tra-1-60, and Tra-1-81 with a differentiation cocktail comprising: GM-CSF and BMP-4.

16. The method of claim 15, further comprising contacting the cell expressing stage specific embryonic antigen 3 (SSEA3), stage specific embryonic antigen 4 (SSEA4) and markers detectable using antibodies designated Tra-1-60, and Tra-1-81 with VEGF.

17. The method of claim 15, further comprising contacting the cell expressing stage specific embryonic antigen 3 (SSEA3), stage specific embryonic antigen 4 (SSEA4) and markers detectable using antibodies designated Tra-1-60, and Tra-1-81 with SCF.