introduce contaminations and make it relatively more expansive to meet good manufacturing process (GMP) requirements.

Accordingly, a need remains for methods and devices to improve cellular expansion, and in particular T-cell expansion, by offering improved bioreactor designs, cost-effective fabrication techniques, and improved bioreactor operating capability in order to achieve clinical application dose requirements.

Summary

A method for T-cell expansion comprises: (a) supplying a 3D bioreactor comprising a plurality of voids having a surface area for cell expansion, said plurality of voids having a diameter **D**, a plurality of pore openings between said voids having a diameter **d**, such that **D>d** and wherein: (a) 90% or more of said voids have a selected void volume (**V**) that does not vary by more than +/- 10.0%; and (b) 90% or more of said pore openings between said voids have a value of **d** that does not vary by more than +/- 10.0%; (b) providing a polydopamine coating on said bioreactor surface area for cell expansion; (c) providing a tetrameric protein, such as avidin or streptavidin, attached to said polydopamine coating; (d) providing one or more biotinylated antibodies immobilized on said tetrameric protein; (e) flowing T-cells through said 3D bioreactor having T-cell surface receptors where said T-cell receptors bind to said biotinylated antibody and are activated; (e) exposing the activated T-cells to a perfusion media containing a signaling molecule (such as cytokine) to promote T-cell expansion.

In one aspect, the present disclosure refers to a method for T-cell expansion comprising: supplying a 3D bioreactor comprising a plurality of interconnected voids having a continuous 3D surface area for cell expansion, said plurality of voids having a diameter **D**, a plurality of pore openings between said voids having a diameter **d**, such that **D>d** and wherein: (a) 90% or more of said voids have a selected void volume (**V**) that does not vary by more than +/- 10.0%; and (b) 90% or more of said pore openings between said voids have a value of **d** that does not vary by more than +/- 10.0%; providing a polydopamine coating on said bioreactor surface area for cell expansion; providing a tetrameric protein attached to said polydopamine coating; providing one or more biotinylated antibodies immobilized on said tetrameric protein; flowing T-cells through said bioreactor having T-cell receptors where said T-cell receptors bind to said one or more biotinylated antibodies and are

Claims:

1. A method for T-cell expansion comprising:

supplying a 3D bioreactor comprising a plurality of interconnected voids having a continuous 3D surface area for cell expansion, said plurality of voids having a diameter **D**, a plurality of pore openings between said voids having a diameter **d**, such that **D>d** and wherein: (a) 90% or more of said voids have a selected void volume (**V**) that does not vary by more than +/- 10.0%; and (b) 90% or more of said pore openings between said voids have a value of **d** that does not vary by more than +/- 10.0%;

providing a polydopamine coating on said bioreactor surface area for cell expansion;

providing a tetrameric protein attached to said polydopamine coating;

providing one or more biotinylated antibodies immobilized on said tetrameric protein;

flowing T-cells through said bioreactor having T-cell receptors where said T-cell receptors bind to said one or more biotinylated antibodies and are activated;

exposing the activated T-cells to a perfusion media containing a signaling molecule to promote T-cell expansion.

2. The method of claim 1 wherein said tetrameric protein comprises avidin or streptavidin.

3. The method of claim 1 wherein said biotinylated antibody comprises anti-CD3 antibody.

4. The method of claim 1 wherein said biotinylated antibody comprises anti-CD3 antibody and anti-CD28 antibody.

5. The method of claim 1 wherein said biotinylated antibody comprises anti-CD3 antibody, anti-CD28 antibody, and anti-CD2 antibody.

6. The method of claim 1 wherein said signaling molecule comprises a cytokine signaling molecule.

7. The method of claim 1 wherein said voids have a diameter (**D**) of greater than 0.4 mm and said pores have a diameter (**d**) of greater than 0.20 mm.

8. The method of claim 1 of claim 1 wherein said voids have a diameter (**D**) in the range of 0.4 mm to 100.0 mm.

9. The method of claim 1 wherein said pores have a diameter (**d**) in the range of 0.2 mm to 10.0 mm.

10. The method of claim 1 wherein 95.0 % or more of said voids indicate a void volume (**V**) that does not vary by more than +/- 10.0%.

11. The method of claim 1 wherein 99.0% to 100% of said voids indicate a void volume (**V**) that does not vary by more than +/- 10.0%.

12. The method of claim 1 wherein 95.0 % or more of said pore openings between said voids have a value of **d** that does not vary by more than +/- 10.0%.

13. The method of claim 1 wherein 99.0 to 100 % of said pore openings between said voids have a value of **d** that does not vary by more than +/- 10.0%.

14. The method of claim 1 wherein at least 90.0% of the voids present have 2 pore openings per void.

15. The method of claim 1 wherein at least 90.0% of the voids present have 8 to 12 pore openings per void.

16. The method of claim 1 wherein said voids have an internal concave surface.

17. The method of claim 1 wherein said voids comprise spherical voids.

18. The method of claim 17 wherein said spherical voids have a packing efficiency of greater than 64.0 % in a 3D cylindrical space.

19. The method of claim 1 wherein said 3D bioreactor is formed from a material that has a Tensile Modulus of at least 0.01 GPa.

20. The method of claim 1 wherein said 3D bioreactor is formed from a material that is biocompatible.

21. The method of claim 1 wherein said 3D bioreactor is formed from a material not susceptible to hydrolysis during cell cultivation such that the amount of hydrolysis does not exceed 5.0 % by weight of the material present.

22. The method of claim 1 wherein said bioreactor has a diameter **Φ** and a height **H** and the ratio **Φ:H** is in the range of greater than 1:1 to 100:1.