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 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%; 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.

Brief Description Of The Drawings

FIG. 1 illustrates a section view of the 3D bioreactor fixed-bed.

FIG. 1a illustrates a unit negative model of the bioreactor that shows the overlapping of the neighborhood spheres.

FIG. 1b illustrates a unit negative model with each sphere surrounded by 12 identical neighborhood spheres.

FIG. 1c illustrates a 3D bioreactor fixed-bed geometry showing an interconnected void system.