extracellular matrix production, and is particularly suitable for the expansion of viral vector producing cells.

In one ~~embodiment~~aspect, the present ~~invention~~disclosure is directed at a method for expansion of viral vector producing cells comprising:

supplying a three-dimensional 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%;

seeding said three-dimensional bioreactor with viral vector producing cells;

flowing a perfusion medium through said three-dimensional bioreactor and promoting viral vector cell expansion.

In another ~~embodiment~~example, the present ~~invention~~disclosure is directed at a 3D bioreactor for growth of viral vector producing cells comprising a plurality of voids having a surface area for cell expansion. The plurality of voids have a diameter **D** of greater than 0.4 mm to 100.0 mm, a plurality of pore openings between the voids having a diameter **d** in the range of 0.2 mm to 10.0 mm, wherein **D>d,** further characterized in that: (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 the pore openings between the voids have a value of **d** that does not vary by more than +/- 10.0%, and the 3D bioreactor is formed from a material having a Tensile Modulus of at least 0.01 GPa.

In a still further ~~embodiment~~example, the present ~~invention~~disclosure is directed at a 3D bioreactor for growth of viral vector producing cells comprising:

a first and second plurality of voids having a surface area for cell expansion;

said first plurality of voids having a diameter $\mathbf{D_1}$, a plurality of pore openings between the first plurality of voids having a diameter $\mathbf{d_1}$, wherein $\mathbf{D_1 > d_1}$, where 90% or more of the plurality of voids have a void volume ($\mathbf{V_1}$) with a tolerance that does not vary by more than +/- 10.0%;

said second plurality of voids having a diameter $\mathbf{D_2}$, a plurality of pore openings between the second plurality of voids having a diameter $\mathbf{d_2}$ wherein $\mathbf{D_2 > d_2}$, wherein 90% of the second plurality of voids have a void volume ($\mathbf{V_2}$) with a tolerance that does not vary by more than +/- 10.0%; and

the values of $\mathbf{V_1}$ and $\mathbf{V_2}$ are different and outside of said tolerance variations such that

$$[\mathbf{V_1} \text{ +/- } 10.0\%] \neq [\mathbf{V_2} \text{ +/- } 10.0\%].$$

The present ~~invention~~disclosure also relates to a fabrication or manufacturing method of forming a 3D bioreactor comprising a plurality of voids having a surface area for viral vector cell expansion. One may therefore initially design/identify for the plurality of voids a targeted internal void volume (V_t) and also identify for the 3D bioreactor a targeted surface area (SA_t). This may then be followed by forming the 3D bioreactor with: (1) an actual void volume (V_a) for the one or more voids wherein V_a is within +/- 10.0% of V_t; and/or (2) an actual surface area (SA_a) of the 3D bioreactor wherein SA_a is within +/- 10.0% of SA_t.

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.

FIG. 1d illustrates a 3D bioreactor fixed-bed geometry in cross-sectional view.

FIG. 1e illustrates in 2D view the identified spherical voids of a 3D bioreactor, and their overlapping areas to form interconnected pores between the spherical voids.