also not conducive to a fast or low-cost process of preparing the cells for introduction to the patient.

BRIEF SUMMARY

[0003] The present disclosure provides methods and systems for replacing or augmenting conventional centrifugation and physical filtration processes along with the multiple washing steps with a simpler, lower cost, and more friendly process for particles such as therapeutic cells. The methods / processes can be performed in a sterile environment and in a continuous form.

[0003a] In a first aspect, the present disclosure provides a method of washing particles, the method comprising: obtaining an initial particle density and volume for an initial mixture of a first media and particles; setting the parameters of an acoustic concentrate wash process using an acoustophoretic device based on the initial particle density and volume of the initial mixture; providing the initial mixture to a chamber of the acoustophoretic device, the acoustophoretic device including at least one ultrasonic transducer that includes a piezoelectric material; driving the at least one ultrasonic transducer to create an acoustic wave in the chamber, such that at least a portion of the particles are retained in an acoustic field generated at least in part by the acoustic wave; and operating the acoustophoretic device in accordance with the parameters.

[0003b] In a second aspect, the present disclosure provides a method of recovering cells from a cell culture, comprising: obtaining an initial particle density and volume for an initial mixture of a first media and particles; setting the parameters of an acoustic concentrate wash process using an acoustophoretic device based on the initial particle density and volume of the initial mixture; feeding the initial mixture of the cell culture to a flow chamber of the acoustophoretic device, the acoustophoretic device including at least one ultrasonic transducer that includes a piezoelectric material that is configured to be driven to generate a multi-dimensional acoustic wave in the flow chamber; and driving the at least one ultrasonic transducer to generate a multi-dimensional acoustic wave in the flow chamber; retaining the cells from the initial mixture in an acoustic field generated at least in part by the multi-dimensional acoustic wave to concentrate the cells; operating the acoustophoretic device in accordance with the parameters.

[0003c] In a third aspect, the present disclosure provides a concentrate wash system, comprising: a pump; a plurality of valves; a flow chamber; at least one ultrasonic transducer coupled to the flow chamber and including a piezoelectric material that is adapted to be driven to generate a multi-dimensional acoustic wave; and a controller for controlling the pump, plurality of valves and at least one ultrasonic transducer, the controller being configurable with parameters that include one or more of acoustic power, flow rate, number of cell collection cycles, number of cells or cell concentration.

[0004] Disclosed herein are methods of washing particles, which may be cells. In some example methods, an initial mixture of a first media and the particles is fed to a flow chamber of an acoustophoretic device. The first media may contain preservatives such as dimethyl sulfoxide (DMSO) which are undesirable for future applications / uses of the particles. The acoustophoretic device has at least one ultrasonic transducer that includes a piezoelectric material and is configured to be driven to create a multi-dimensional acoustic standing wave in the flow chamber. At least a portion of the particles are trapped in the multi-dimensional acoustic standing wave. A second media is flowed through the flow chamber to wash out the first media while the particles are retained in the multidimensional acoustic standing wave. The particles may thus experience a media exchange, where the first media is exchanged for the second media.

[0005] In some examples, the volume of the second media used to perform the wash process may be equivalent to a volume of the flow chamber. In some examples, the volume of the second media used to perform the wash process may be multiples of or portions of the volume of the flow chamber. The second media can be a biocompatible wash or a buffer solution.

[0006] The particles may be cells. The cells may be Chinese hamster ovary (CHO) cells, NS0 hybridoma cells, baby hamster kidney (BHK) cells, human cells, regulatory T-cells, Jurkat T-cells, CAR-T cells, B cells, or NK cells, peripheral blood mononuclear cells (PBMCs), algae, plant cells, bacteria, or viruses. The cells may be attached to microcarriers.

[0007] Sometimes, the piezoelectric material of the at least one ultrasonic transducer is in the form of a piezoelectric array formed from a plurality of piezoelectric elements. Each piezoelectric element can be physically separated from surrounding

CLAIMS:

1. A method of washing particles, the method comprising:

obtaining an initial particle density and volume for an initial mixture of a first media and particles;

setting the parameters of an acoustic concentrate wash process using an acoustophoretic device based on the initial particle density and volume of the initial mixture;

providing the initial mixture to a chamber of the acoustophoretic device, the acoustophoretic device including at least one ultrasonic transducer that includes a piezoelectric material;

driving the at least one ultrasonic transducer to create an acoustic wave in the chamber, such that at least a portion of the particles are retained in an acoustic field generated at least in part by the acoustic wave; and

operating the acoustophoretic device in accordance with the parameters.

2. The method of claim 1, further comprising providing a second media to the chamber that is a biocompatible wash or a buffer solution.

3. The method of claim 1, wherein the particles are cells.

4. The method of claim 1, wherein the particles are microcarrier/cell complexes.

5. The method of claim 1, wherein the initial mixture has a density of about 0.5 million particles/mL to about 5 million particles/mL.

6. The method of claim 1, further comprising concentrating the particles in the initial mixture.

7. The method of claim 1, further comprising concentrating the particles to a concentrate volume that is about 25 to about 50 times less than a volume of the initial mixture.

8. The method of claim 7, further comprising concentrating the particles in the initial mixture to a concentrated particle density of about 25 to about 50 times greater than a particle density of the initial mixture.

9. The method of claim 1, wherein a cell density of a wash output of the flow chamber is about 0.0 to about 0.5 million cells/mL.

10. The method of claim 9, wherein the wash output is from a concentrate process and a wash process.

11. The method of claim 1, further comprising conducting a spectrophotometer process on the chamber to determine wash efficacy.

12. A method of recovering cells from a cell culture, comprising:

obtaining an initial particle density and volume for an initial mixture of a first media and particles;

setting the parameters of an acoustic concentrate wash process using an acoustophoretic device based on the initial particle density and volume of the initial mixture;

feeding the initial mixture of the cell culture to a flow chamber of the acoustophoretic device, the acoustophoretic device including at least one ultrasonic transducer that includes a piezoelectric material that is configured to be driven to generate a multi-dimensional acoustic wave in the flow chamber; and

driving the at least one ultrasonic transducer to generate a multi-dimensional acoustic wave in the flow chamber;

retaining the cells from the initial mixture in an acoustic field generated at least in part by the multi-dimensional acoustic wave to concentrate the cells;

operating the acoustophoretic device in accordance with the parameters.

13. The method of claim 12, wherein the cell density of the concentrated cells is about 25 to about 50 times greater than the cell density of the initial mixture.

14. The method of claim 12, wherein a volume of the concentrated cells is 25 to about 50 times less than a volume of the initial mixture.

15. The method of claim 12, wherein the concentrated cells are obtained in about 35 minutes or less.

16. The method of claim 12, further comprising washing the concentrated cells, wherein a cell density of a wash output of the flow chamber is about 0.0 to about 0.5 million cells/mL.

17. A concentrate wash system, comprising:

a pump;

a plurality of valves;

a flow chamber;

at least one ultrasonic transducer coupled to the flow chamber and including a piezoelectric material that is adapted to be driven to generate a multi-dimensional acoustic wave; and

a controller for controlling the pump, plurality of valves and at least one ultrasonic transducer, the controller being configurable with parameters that include one or more of acoustic power, flow rate, number of cell collection cycles, number of cells or cell concentration.

18. The concentrate wash system of claim 17, wherein the flow chamber further comprises a volume of about 25 mL to about 75 mL.

19. The concentrate wash system of claim 18, wherein the flow chamber can contain a cell capacity of about 4 billion to about 40 billion cells.