CLAIMS

1. A cell processing system comprising:
at least one cell suspension module;
at least one buffer module;
at least one flow-through magnetic separation/debeading module;
at least one non-magnetic output module; and
at least one magnetic output module.

2. The cell processing system of Claim 1, further comprising at least one return loop returning upstream of at least one flow-through magnetic separation/debeading module.

3. The cell processing system of Claim 1, comprising at least two flow-through magnetic separation/debeading modules in parallel or in series.

4. The cell processing system of Claim 1, further comprising at least one additional module.

5. The cell processing system of Claim 4, wherein the at least one additional module comprises at least one spinning membrane debeading module.

6. The cell processing system of Claim 5, comprising at least two spinning membrane debeading modules in parallel or in series.

7. The cell processing system of Claim 4, wherein the at least one additional module comprises at least one physical separation module.

8. The cell processing system of Claim 7, wherein the at least one additional module comprises at least one magnetic column module.

9. The cell processing system of Claim 4, wherein the at least one additional module comprises one of the following: at least one media exchange module, at least one cell concentration module and at least one cell washing module.

10. The cell processing system of Claim 1, wherein the flow-through magnetic separation/debeading module comprises:

a chamber defined by walls and having an x-direction, a y-direction, and a z-direction;

an inlet and an outlet arranged on opposite ends of the chamber in the y-direction; and

at least two magnets adjacent or proximate a wall of the chamber and arranged to establish a zero gradient line within the chamber between the inlet and the outlet.

11. The cell processing system of Claim 5, wherein the spinning membrane debeading module comprises:

a debeading chamber define partially by a cylindrical side-wall;

a porous spinning membrane having an interior and oriented co-axially with the cylindrical side-wall;

a sample inlet;

a waste output module connected to the interior of the spinning membrane; and

a cell output module connected to the debeading chamber.

12. The cell processing system of Claim 11, wherein the spinning membrane debeading module further comprises at least one magnet adjacent or proximate to the cylindrical side-wall.

13. A flow-through magnetic separation/debeading module comprising:

a chamber defined by walls and having an x-direction, a y-direction, and a z-direction;

an inlet and an outlet arranged on opposite ends of the chamber in the y-direction; and

at least two magnets adjacent or proximate a wall of the chamber and arranged to establish a zero gradient line within the chamber between the inlet and the outlet.

14. The module of Claim 13, comprising at least two inlets and at least two outlets.

15. The module of Claim 13, further comprising at least three magnets adjacent or proximate a wall of the chamber and arranged to establish at least two zero gradient lines within the chamber between the inlet and the outlet; or further comprising at least four magnets arranged in two arrays on opposite sides of the chamber in the z-direction.

16. The module of Claim 14, further comprising at least four magnets arranged in two arrays on opposite side of the chamber in the z-direction and cross-oriented in the x-y plane from near one inlet to near one outlet on the opposite side of the chamber in the z-direction.

17. The module of Claim 13, further comprising:

sub-membrane injection ports adjacent a wall of the chamber also adjacent at least two magnets; and

a membrane adjacent the sub-membrane.

18. A spinning membrane debeading module comprising:

a debeading chamber define partially by a cylindrical side-wall;

a porous spinning membrane having an interior and oriented co-axially with the cylindrical side-wall;

a sample inlet;

a waste output module connected to the interior of the spinning membrane;

a cell output module connected to the debeading chamber; and

at least one magnet adjacent or proximate to the cylindrical side-wall.

19. The spinning membrane debeading module of Claim 18, further comprising a reagent module; or wherein the porous spinning membrane has a pore size greater than that of a particle to be debeaded and less than that of a cell to be debeaded.

20. A method of flow-through cell processing comprising flowing a cell suspension comprising paramagnetic particle-bound cells through a flow-through magnetic separation/debeading module to produce an unbound cell product,

wherein the paramagnetic particle-bound cells continue to move in the flow-through magnetic separation/debeading module through the flowing step, and

wherein the flow-through magnetic separation/debeading module comprises:

a flow chamber defined by walls through which the cell suspension flows; and

at least two magnets arranged adjacent or proximate at least one wall.

21. The method of Claim 20, wherein the cell suspension is flowed laminarly through the flow-through magnetic separation/debeading module; or wherein the magnets are oriented to establish one zero gradient line that crosses the direction of flow, such that paramagnetic-particle bound cells are pulled to the zero gradient line in one direction only, but are not affected by magnetic forces of the two magnets in two other directions.

22. The method of Claim 20, wherein the cell suspension further comprises unbound cells and flowing the cell suspension through the flow-through magnetic separation/debeading module separates the paramagnetic particle-bound cells and the unbound cells.

23. The method of Claim 22, wherein the cell suspension further comprises free paramagnetic particles and flowing the cell suspension through the flow-through magnetic separation/debeading module separates the free paramagnetic particles and the unbound cells; or further comprising flowing the separated unbound cells through the flow-through magnetic separation/debeading module a second or subsequent time using a return loop.

24. The method of Claim 22, further comprising flowing the separated paramagnetic particle-bound cells through the flow-through magnetic separation/debeading module a second or subsequent time using a return loop.

25. The method of Claim 24, further comprising debeading the paramagnetic particle-bound cells in the flow-through magnetic separation/debeading module during the second or subsequent time to produce paramagnetic particles and debeaded, unbound cells.

26. The method of Claim 25, further comprising flowing the produced paramagnetic particles and debeaded, unbound cells through the flow-through magnetic separation/debeading module a third or subsequent time to separate the paramagnetic particles and the debeaded, unbound cells.

27. The method of Claim 20, wherein the chamber further comprises:

a magnetic inlet through which any paramagnetic particles enter the flow chamber;

a non-magnetic inlet;

a magnetic outlet opposite the non-magnetic inlet; and

a non-magnetic outlet opposite the magnetic inlet, wherein the zero gradient line directs all paramagnetic particles and any bound cells to the magnetic outlet.

28. The method of Claim 27, wherein the cell suspension further comprises unbound cells;

wherein the non-magnetic inlet is larger than the magnetic inlet and the non-magnetic outlet is larger than magnetic outlet, wherein fluid flowing from the non-magnetic inlet crosses over to the non-magnetic outlet, preventing any unbound cells from flowing into the magnetic outlet;

or wherein the non-magnetic inlet and magnetic inlet are substantially the same size or the non-magnetic outlet and magnetic outlet are substantially the same size, or both, and wherein respective flow rates of the fluid enter the inlets, the respective flow rates of the fluid exiting the outlets, or both are adjusted such that fluid flowing from the non-magnetic inlet crosses over to the non-magnetic outlet, preventing any unbound cells from flowing into the magnetic outlet.

29. The method of Claim 20, further comprising flowing the paramagnetic particle-bound cells through a spinning membrane debeading module to produce the unbound cell product, wherein the spinning membrane debeading module comprises:

a cylindrical debeading chamber through which the paramagnetic particle-bound cells flow, the chamber defined in part by a cylindrical side-wall and containing a co-axial spinning membrane; and

at least one magnet arranged adjacent or proximate the cylindrical side-wall to establish at least one zero gradient line within the cylindrical debeading chamber.

30. The method of Claim 20, further comprising flowing the paramagnetic particle-bound cells through a magnetic column module to produce the unbound cell product; or further comprising flowing the paramagnetic particle-bound cells or the unbound cell product through one of the following: a cell washing module, a media exchange module and a cell concentration module.

31. A method of manufacturing a cell therapy composition, said method comprising:

contacting a cell population with paramagnetic particles coated with one or more agents which assist in expanding one or more cell types within the cell population;

introducing nucleic acid into cells within the cell population;

expanding cells within the cell population;

debeading the cell population according to the method of any of Claims 20 to 30, or using the system of any of Claims 1 to 12 or the module of any of Claims 13 to 19; and

formulating the cell population for cell therapy.

32. The method of Claim 31, wherein the one or more agents which assist in expanding one or more cell types comprises anti-CD3 antibody or antigen binding fragment thereof, anti-CD28 antibody or antigen binding fragment thereof, and combinations thereof.

33. The method of any of Claims 31 or 32, wherein the nucleic acid is introduced by lentivirus or mRNA transduction.

34. The method of any of Claims 31 to 33, wherein the cell therapy is a chimeric antigen receptor T cell therapy.

35. The method of claim 34, wherein the cell therapy is an anti-CD19 chimeric antigen receptor T cell therapy.