CLAIMS:

1. A cell culture system comprising:

a first area configured to receive a fluid reservoir comprising a cell culture medium;

a second area configured to receive a waste reservoir;

one or more pumps fluidically connectable to the fluid reservoir; and

a substrate configured to receive and retain cell culture chambers of different shapes and/or sizes.

2. The cell culture system of claim 1, wherein the substrate comprises a plurality of different openings in the substrate that are arranged such that the substrate is configured to simultaneously receive and retain multiple cell culture chambers of different shapes and/or sizes.

~~3. The cell culture system of claim 1, wherein the substrate is configured to receive and retain multiple cell culture chambers simultaneously~~.

3~~4~~. The cell culture system of claim 1, further comprising the fluid reservoir positioned in the first area and the waste reservoir positioned in the waste area.

4~~5~~. The cell culture system of claim 3~~4~~, further comprising one or more tubes that fluidically connect from fluid reservoir to the one or more pumps, from the one or more pumps to the cell culture chambers, and from the cell culture chambers to the waste reservoir.

5~~6~~. The cell culture system of claim 1, wherein a first portion of the substrate is configured to receive a first cell culture chamber of a first size and/or shape, and a second portion of the substrate is configured to receive a second cell culture chamber of a second size and/or shape which is different from the first size and/or shape.

~~7. The cell culture system of claim 1, wherein a first portion of the substrate is configured to receive a first cell culture chamber of a first shape and a second portion of the substrate is~~

~~configured to receive a second cell culture chamber of a second shape that is different from the first shape.~~

~~8. The cell culture system of claim 1, wherein a first portion of the substrate is configured to receive a first cell culture chamber of a first size and shape and a second portion of the substrate is configured to receive a second cell culture chamber of a second size and shape that is different from the first size and shape.~~

6~~9~~. The cell culture system of claim 1, wherein each cell culture chamber is fluidically coupled to a separate pump.

7~~10~~. The cell culture system of claim 1, further comprising a processor operably connected to the one or more pumps and one or more sensors operable to measure a characteristic of a fluid in the cell culture system, wherein the processor operates the one or more pumps based on the measured characteristic.

8~~11~~. A method for culturing cells, the method comprising:

providing cell culture system comprising a first area configured to receive a fluid reservoir comprising a cell culture medium a second area configured to receive a waste reservoir, one or more pumps fluidically connectable to the fluid reservoir, and a substrate configured to receive and retain cell culture chambers of different shapes and/or sizes;

loading the fluid reservoir into the first area and the waste reservoir into the second area;

loading a first cell culture chamber of a first size and/or shape onto a first portion of the substrate;

loading a second cell culture chamber of a second size and/or shape onto a second portion of the substrate;

connecting the fluid reservoir, the one or more pumps, the first and second cell culture chambers, and the waste reservoir with tubing; and

operating the system to culture cells in the first and second cell culture chambers.

9~~12~~. The method of claim 8~~11~~, wherein the substrate comprises a plurality of different openings in the substrate that are arranged such that the substrate is configured to simultaneously receive and retain multiple cell culture chambers of different shapes and/or sizes.

10~~13~~. The method of claim 8~~11~~, wherein the first cell culture chamber is of a first size and/or shape, and the second cell culture chamber is of a second size and/or shape.

~~14. The method of claim 11, wherein the first cell culture chamber is of a first shape and the second cell culture chamber is of a second shape.~~

~~15. The method of claim 11, wherein the first cell culture chamber is of a first size and shape and the second cell culture chamber is of a second size and shape.~~

11~~16~~. The method of claim 8~~11~~, wherein each of the first and second cell culture chambers is fluidically coupled to a separate pump.

12~~17~~. The method of claim 8~~11~~, wherein the cell culture system further comprises a processor operably connected to the one or more pumps and one or more sensors operable to measure a characteristic of a fluid in the cell culture system, wherein the processor operates the one or more pumps based on the measured characteristic.

13~~18~~. The method of claim 8~~11~~, wherein after cell culturing is complete in the first and second cell culture chambers, the cultured cells in each of the first and second cell culture chambers are collected.

14~~19~~. The method of claim 13~~18~~, wherein the cultured cells in each of the first and second cell culture chambers are collected in the same collection vessel.

15~~20~~. The method of claim 13~~18~~, wherein the cultured cells in each of the first and second cell culture chambers are collected in different collection vessels.

~~21. A method for producing transduced T cells, the method comprising:~~

~~providing a cell culture instrument that comprises first and second culture chambers;~~

~~flowing a suspension comprising T cells into the first culture chamber ;~~

~~perfusing the T cells in the first culture chamber to produce transduced T cells which expand in the first culture chamber;~~

~~flowing the transduced and expanded T cells from the first culture chamber into the second culture chamber; and~~

~~flowing a cell culture medium into the second culture chamber to further expand the tranduced and expanded T cells, wherein the method is performed on a single instrument in a closed manner such that sterility is maintained throughout the method.~~

~~22. The method of claim 21, wherein the second culture chamber is larger than the first culture chamber.~~

~~23. The method of claim 21, wherein the first and second culture chambers are made of polystyrene.~~

~~24. The method of claim 21, wherein the first and second culture chambers are connected via a sterile tube.~~

~~25. The method of claim 21, wherein the first culture chamber further comprises an activation reagent and/or a cell transduction reagent.~~

~~26. The method of claim 25, wherein the cell transduction reagent comprises an inactive virus expressing CAR or TCR.~~

~~27. The method of claim 21, wherein the cell culture medium is provided in sterile vessel and is connected to the closed system by sterile tube welding.~~

~~28. The method of claim 21, wherein flowing the cell culture medium into the first culture chamber comprises eliminating headspace in the first culture chamber.~~

~~29. The method of claim 21, further comprising activating the T cells in the first culture chamber.~~

~~30. The method of claim 29, wherein activating comprises contacting with a reagent comprising an antibody.~~

~~31. The method of claim 30, wherein the antibody is attached to a bead.~~

~~32. The method of claim 21, further comprising:~~
~~draining fluid from the second culture chamber;~~
~~washing the transduced and expanded T cells with a buffer; and~~
~~flowing a cryopreservation medium into the second culture chamber to re-suspend the transduced and expanded T cells.~~

~~33. The method of claim 21, further comprising flowing the transduced and expanded T cells into a harvesting vessel in a closed manner.~~

~~34. The method of claim 21, wherein each of the flowing steps is done via sterile tubes.~~

~~35. The method of claim 34, wherein the sterile tubes are connected by sterile tube welding.~~

~~36. The method of claim 21, wherein the cell culture medium comprises Aim V with interleukin-2.~~

~~37. A method for producing neo-antigen transduced T cells, the method comprising:~~
~~providing a cell culture instrument comprising first and second culture chambers;~~
~~flowing cell culture medium containing monocytes into the first culture chamber;~~

perfusing the purified monocytes in the first culture chamber to produce dendritic cells in the first culture chamber;

contacting the dendritic cells with antigen material in the first culture chamber to produce mature dendritic cells;

flowing a cell suspension comprising T cells into the first culture chamber to co-culture the mature dendritic cells and the T cells, to thereby produce expanded neoantigen-targeting T cells;

wherein the method is performed on a single instrument in a closed manner such that sterility is maintained throughout the method.

38. The method of claim 37, further comprising:

generating a second batch of mature dendritic cells in the second culture chamber; and

introducing the expanded T cells from the first culture chamber into the second culture chamber to co-culture the expanded T cells with the second batch of mature dendritic cells.

39. The method of claim 38, wherein the second batch of mature dendritic cells have been stimulated with a different set of peptides than the mature dendritic cells from the first culture chamber.

40. The method of claim 38, further comprising:

transferring the expanded T cells that have been co-cultured with the second batch of mature dendritic cells back to the first culture chamber comprising, wherein the first culture chamber comprises a third batch of mature dendritic cells.

41. The method of claim 37, wherein the antigen material comprises tumor-specific peptides.

42. The method of claim 37, wherein the first and second culture chambers are made of polystyrene.

43. The method of claim 37, wherein the first and second culture chambers are connected via a sterile tube.

44. The method of claim 37, wherein the cell culture medium is provided in sterile vessel and is connected to the closed system by sterile tube welding.

45. The method of claim 37, wherein flowing the cell culture medium into the first culture chamber comprises eliminating headspace in the first culture chamber.

46. The method of claim 37, further comprising:

draining fluid from the first culture chamber;

washing the neo-antigen transduced T cells with a buffer; and

flowing a cryopreservation medium into the first culture chamber to re-suspend the neo-antigen transduced T cells.

47. The method of claim 37, further comprising flowing the neo-antigen transduced T cells into a harvesting vessel in a closed manner.

48. The method of claim 37, wherein each of the flowing steps is done via sterile tubes.

49. The method of claim 48, wherein the sterile tubes are connected by sterile tube welding.

50. A method for producing dendritic cells and stimulating T cells in parallel, the method comprising:

providing a cell culture instrument comprising first and second culture chambers;

flowing cell culture medium comprising monocytes into the first culture chamber;

perfusing the monocytes in the first culture chamber to produce dendritic cells in the first culture chamber;

flowing a cell suspension comprising T cells into the first culture chamber to co-culture the dendritic cells and the T cells, to thereby produce activated expanded T cells; and

flowing the activated expanded T cells from the first culture chamber into the second culture chamber comprising dendritic cells generated from a second, separate batch of monocytes to further culture the T cells.

51. The method of claim 50, wherein sterility is maintained throughout the method.

52. The method of claim 50, wherein the method further comprises collecting the cultured T cells from the first culture chamber by flowing the cultured T cells into a collection vessel.

53. The method of claim 50, further comprising maturing the dendritic cells in the first culture chamber by contacting the dendritic cells with antigen material.

54. The method of claim 53, wherein the antigen material comprises tumor-specific peptides.

55. The method of claim 50, wherein the first and second culture chambers are made of polystyrene.

56. The method of claim 50, wherein the first and second culture chambers are connected via a sterile tube.

57. The method of claim 50, wherein the cell culture medium is provided in a sterile vessel and is connected to the closed system by sterile tube welding.

58. The method of claim 50, wherein flowing the cell culture medium into the first culture chamber comprises eliminating headspace in the first culture chamber.

59. The method of claim 50, further comprising activating the T cells in the second culture chamber.

60. The method of claim 59, wherein activating comprises contacting with a reagent comprising an antibody.

61. The method of claim 50, further comprising washing the stimulated T cells with a buffer.

~~62. The method of claim 61, further comprising transferring the stimulated T cells to a cryopreservation medium.~~

~~63. The method of claim 50, further comprising flowing the neo-antigen transduced T cells into a harvesting vessel in a closed manner.~~

~~64. The method of claim 50, wherein each of the flowing steps is done via sterile tubes.~~

~~65. The method of claim 64, wherein the sterile tubes are connected by sterile tube welding.~~

~~66. The method of claim 50, wherein either or both of the first and second cell culture chambers from the cell culture instrument are replaced and the method is repeated.~~

~~67. A cell culture chamber wherein a top, a bottom, and both side walls are comprised of a gas-impermeable material.~~

~~68. The cell culture chamber of claim 67, wherein the gas-impermeable material is also a material to which cells adhere.~~

~~69. The cell culture chamber of claim 68, wherein the gas-impermeable material comprises polystyrene.~~

~~70. The cell culture chamber of claim 67, wherein the cell culture chamber further comprises an inlet.~~

~~71. The cell culture chamber of claim 70, wherein the cell culture chamber further comprises an outlet.~~

~~72. The cell culture chamber of claim 71, wherein the inlet and the outlet are located on the top of the cell culture chamber.~~

~~73. The cell culture chamber of claim 72, wherein the inlet and the outlet are each configured to fluidically and sealably couple with tubing.~~

~~74. The cell culture chamber of claim 67, wherein the cell culture chamber is integrally formed.~~

~~75. The cell culture chamber of claim 67, wherein the cell culture chamber is sized and configured to fit within an incubator.~~

~~76. The cell culture chamber of claim 67, wherein the cell culture chamber is sized and configured to couple to a substrate of a cell culture instrument.~~

~~77. A method for culturing cells, the method comprising:~~

~~providing a cell culture chamber comprising an inlet and an outlet, wherein a top, a bottom, and both side walls are comprised of a gas-impermeable material;~~

~~loading cells into the cell culture chamber; and~~

~~flowing a cell culture medium into the cell culture chamber via the inlet to culture the cells in the culture chamber and out of the cell culture chamber via the outlet, wherein the flowing of the cell culture medium through the cell culture chamber via the inlet and the outlet causes continuous flow of cell culture medium through the cell culture chamber and allows for gas exchange to occur between the cells in the cell culture chamber and the cell culture medium.~~

~~78. The method of claim 77, wherein the gas-impermeable material is also a material to which cells adhere.~~

~~79. The method of claim 78, wherein the gas-impermeable material comprises polystyrene.~~

~~80. The method of claim 77, wherein the inlet and the outlet are located on the top of the cell culture chamber.~~

~~81. The method of claim 80, wherein the inlet and the outlet are fluidically and sealably couple with tubing.~~

~~82. The method of claim 77, wherein the cell culture chamber is integrally formed.~~

~~83. The method of claim 77, wherein the cell culture chamber is sized and configured to fit within an incubator.~~

~~84. The method of claim 77, wherein the cell culture chamber is sized and configured to couple to a substrate of a cell culture instrument.~~

~~85. The method of claim 81, wherein the tubing is high permeability tubing.~~

~~86. The method of claim 85, wherein the cell culture medium exchanges gas while in the high permeability tubing.~~

~~87. A method for culturing cells, the method comprising:~~

~~culturing cells in a cell culture chamber on a cell culture instrument by flowing a cell culture medium through the cell culture chamber, wherein a portion of the cell culture medium that has already been flowed through the cell culture chamber is recycled back into the cell culture chamber during the cell culturing process.~~

~~88. The method of claim 87, further comprising measuring one or more parameters of the used medium prior to the recycling.~~

~~89. The method of claim 88, wherein at least one of the one or more parameters comprises a concentration of one or more compounds within the used medium.~~

~~90. The method of claim 89, wherein the one or more compounds comprise glucose, lactate, dissolved oxygen, or cell metabolites.~~

~~91. The method of claim 88, wherein the parameter comprises pH.~~

92. The method of claim 88, further comprising determining, using a processor operably connected to the cell culture chamber, whether at least one of the one or more parameters of the used medium meets a predetermined threshold prior to the recycling step.

93. The method of claim 88, wherein the measuring step is performed by one or more sensors operably associated with the cell culture chamber.

94. The method of claim 93, wherein the one or more sensors are operably associated with a waste reservoir in fluid communication with the cell culture chamber.

95. The method of claim 94, wherein the recycling step comprises redirecting the portion of used medium from the waste reservoir back into the cell culture chamber.

96. The method of claim 87, further comprising combining the portion of used medium with a bolus of fresh medium.

97. The method of claim 87, wherein the cell culture chamber is operably connected to one or more pumps.

98. The method of claim 87, wherein the cell culture chamber comprises an inlet and an outlet.

99. A method for culturing cells, the method comprising:

providing a cell culture chamber comprising cells;

flowing a cell culture medium into the cell culture chamber;

removing used cell culture medium from the cell culture chamber;

assessing a parameter of the used cell culture medium; and

returning the used cell culture medium to the cell culture chamber if the parameter meets a predetermined threshold.

100. The method of claim 99, further comprising combining the used cell culture medium with a bolus of fresh cell culture medium prior to the returning step.

101. The method of claim 99, wherein the assessing step comprises measuring the parameter using a sensor operably coupled to the cell culture chamber.

102. The method of claim 99, wherein the assessing step comprises determining, using a processor, whether the parameter meets the predetermined threshold.

103. The method of claim 102, wherein the parameter comprises a measured concentration of one or more compounds within the used cell culture medium.

104. The method of claim 103, wherein the one or more compounds comprise glucose, lactate, or cell metabolites.

105. The method of claim 99, wherein the returning step comprises redirecting the used cell culture medium from a waste reservoir into the cell culture chamber.

106. The method of claim 99, further comprising:

discarding the used cell culture medium if the parameter does not meet the predetermined threshold; and

flowing fresh cell culture medium into the cell culture chamber.

107. A cell culture system, the system comprising:

a plurality of shelves stacked with a first shelf on top of a second shelf, each of the first and second shelves configured to receive a fluid reservoir;

at least one pump;

a processor operably coupled to the at least one pump; and

a substrate sized and configured to hold a plurality of cell culture chambers at a same time.

108. The system of claim 107, wherein the system comprises at least one sensor.

~~109. The system of claim 108, wherein the processor is connectable to at least one sensor and is configured to operate the at least one pump based on a characteristic measured by the sensor.~~

~~110. The system of claim 107, wherein the substrate is configured to receive cell culture chambers of different sizes and/or shapes.~~

~~111. The system of claim 107, wherein the at least one pump is a plurality of pumps.~~

~~112. The system of claim 111, further comprising a plurality of tubes that fluidically connect from a first fluid reservoir on the first shelf to the plurality of pumps, from the plurality of pumps to a plurality of cell culture chambers, and from the plurality of cell culture chambers to a second fluid reservoir on the second shelf.~~

~~113. The system of claim 107, wherein each of the first and second shelves comprises a retaining mechanism that retains the fluid reservoir on each of the first and second shelves.~~

~~114. The system of claim 107, wherein the system is dimensioned for insertion into an incubator.~~

~~115. The system of claim 107, wherein the processor is configured to receive and execute instructions for culturing a cell type.~~

~~116. The system of claim 107, wherein the processor is configured to receive and execute instructions for transducing T cells.~~

~~117. A cell culture method, the method comprising:~~

~~providing a cell culture system comprising a plurality of shelves stacked with a first shelf on top of a second shelf, each of the first and second shelves configured to receive a fluid reservoir; at least one pump; a processor operably coupled to the at least one pump; and a substrate sized and configured to hold a plurality of cell culture chambers at a same time;~~

~~loading a first fluid reservoir onto the first shelf;~~

~~loading a second fluid reservoir onto the second shelf;~~

~~loading a first cell culture chamber and a second cell culture chamber onto the substrate;~~

~~connecting the fluid and second fluid reservoirs, the at least one pump, and the first and second cell culture chambers, with tubing; and~~

~~operating the system to culture cells inside the first and second cell culture chambers.~~

~~118. The method of claim 117, wherein the first and the second cell culture chambers comprise different sizes or shapes.~~

~~119. The method of claim 117, wherein the system comprises at least one sensor.~~

~~120. The method of claim 119, wherein the processor is connected to at least one sensor and is configured to operate the pump based on a characteristic measured by the sensor.~~