Bedside Automated Cell Engineering System and Methods

Field of the Invention

[0001] The present disclosure provides cell therapy production systems that can suitably be used in a patient bedside setting. Such systems allow for direct removal of a patient's blood, automated processing to produce a cell therapy, and then infusion back into the patient, without the need to remove the system from the patient's bedside. Also provided herein are systems for production of cell therapies in a bedside setting.

Background of the Invention

[0002] As anticipation builds about accelerated clinical adoption of advanced cell therapies, more attention is turning to the underlying manufacturing strategies that will allow these therapies to benefit patients worldwide. While cell therapies hold great promise clinically, high manufacturing costs relative to reimbursement present a formidable roadblock to commercialization. Thus, the need for cost effectiveness, process efficiency and product consistency is driving efforts for automation in numerous cell therapy fields.

[0003] Automation of various processes is involved in producing cell populations for therapy. This includes integration of cell activation, transduction and expansion into a commercial manufacturing platform for the translation of these important therapies to the broad patient population.

[0004] In addition, it is highly desirable to have cell production processes be performed directly at a patient's bedside for easy and fast therapeutic applications. However, such systems must not only maintain the necessary automated processing, but also ensure sterility of the therapy and also control over the process. The present invention fulfills these needs.

Summary

[0005] In one ~~aspect~~example, the present disclosure refers to a cell therapy production system, comprising: (a) a blood withdrawal device; (b) a cell separation device fluidly connected to the

blood withdrawal device; (c) a cell transduction apparatus fluidly connected to the cell separation filter; (d) a cell processing apparatus fluidly connected to the cell transduction apparatus; and (e) a cell therapy infusion device fluidly connected to the cell processing apparatus.

[0005a] In one aspect, the present disclosure refers to a cell therapy production system, comprising: (a) a blood withdrawal device; (b) a cell separation device fluidly connected to the blood withdrawal device; (c) a cell transduction apparatus fluidly connected to the cell separation device; (d) a cell processing apparatus for processing a cell therapy, the cell processing apparatus being fluidly connected to the cell transduction apparatus and to a patient; (e) a cell therapy infusion device capable of returning the cell therapy to the patient, the cell therapy infusion device being fluidly connected to the cell processing apparatus; and (f) an automated process control system configured to automatically control the cell therapy production system.

[0006] In another ~~aspect~~example, the present disclosure refers to a cell therapy production system, comprising: (a) a blood withdrawal device; (b) an automated cell engineering system, including: i. an enclosable housing; ii. a cell separation device contained within the enclosable housing and fluidly connected to the blood withdrawal device; iii. a cell transduction apparatus contained within the enclosable housing and fluidly connected to the cell separation filter; and iv. a cassette contained within the enclosable housing, the cassette comprising a cell culture chamber fluidly connected to the cell transduction apparatus; and (c) a cell therapy infusion device fluidly connected to the cell culture chamber.

[0006a] In one aspect, the present disclosure refers to a cell therapy production system, comprising: (a) a blood withdrawal device; (b) an automated cell engineering system, including: i. an enclosable housing; ii. a cell separation device contained within the enclosable housing and fluidly connected to the blood withdrawal device; iii. a cell transduction apparatus contained within the enclosable housing and fluidly connected to the cell separation device; and iv. a cassette contained within the enclosable housing, the cassette comprising a low temperature chamber for storage of a cell culture media, and a high temperature chamber that includes a cell culture chamber fluidly connected to the cell transduction apparatus; (c) an automated process control system configured to automatically control the cell therapy production system; and (d) a cell therapy infusion device capable of returning the cell therapy to a patient, the cell therapy infusion device being fluidly connected to the cell culture chamber.

[0007] Also provided herein is a method for preparing a cell therapy product, the method comprising: withdrawing a blood sample from a patient; passing the blood sample through a cell separation device to remove a target cell population from the blood sample; transducing the target cell population with a vector to produce a transduced cell culture; optionally expanding the transduced cell culture; harvesting the cell culture; and infusing the harvested cell culture into the patient.

~~**[0007a]** In another aspect, the present disclosure refers to a method for preparing a cell therapy product, the method comprising: (a) passing a blood sample withdrawn from a patient through a cell separation device to remove a target cell population from the blood sample; (b) transducing the target cell population with a vector to produce a transduced cell culture; (c) optionally expanding the transduced cell culture; and (d) harvesting the cell culture; wherein the harvested cell culture is to be infused into the patient.~~

Brief Description of the Figures

[0008] FIG. 1 shows a cell therapy production system in accordance with embodiments hereof.

[0009] FIG. 2 shows exemplary components of a call therapy production system in accordance with embodiments hereof.

[0010] FIGS. 3A-3B show an automated cell engineering system in accordance with embodiments hereof.

[0011] FIG. 4 shows a cartridge for use in embodiments hereof.

CLAIMS

1. A cell therapy production system, comprising:

(a) a blood withdrawal device;

(b) a cell separation device fluidly connected to the blood withdrawal device;

(c) a cell transduction apparatus fluidly connected to the cell separation devicefilter;

(d) a cell processing apparatus for processing a cell therapy, the cell processing apparatus being fluidly connected to the cell transduction apparatus and to a patient; and

(e) a cell therapy infusion device capable of returning the cell therapy to the patient, the cell therapy infusion device being fluidly connected to the cell processing apparatus; and

(f) an automated process control system configured to automatically control the cell therapy production system.

2. The system of claim 1, wherein the cell separation device is a cell separation filter that includes a matrix which captures a target cell population.

3. The system of claim 2, wherein the target cell population is a T-cell population.

4. The system of any one of claims 1-3, wherein the cell transduction apparatus is an electroporation unit.

5. The system of any one of claims 1-4, wherein the cell separation devicefilter, the cell transduction apparatus and the cell processing apparatus are contained within an automated cell engineering system.

6. The system of any one of claims 1-5, wherein the cell processing apparatus includes a cell culture chamber.

7. The system of any one of claims 5-6, wherein the automated cell engineering system includes an enclosable housing.

8. The system of claim 6, further comprising one or more fluidics pathways, wherein the fluidics pathways provide recirculation, removal of waste and homogenous gas exchange and distribution of nutrients to the cell culture chamber without disturbing cells within the cell culture chamber.

9. The system of any one of claims 1-8, further comprising one or more of a pH sensor, a glucose sensor, an oxygen sensor, a carbon dioxide sensor, and/or an optical density sensor.

10. The system of any one of claims 1-9, wherein the system is portable.

~~11. The system of any one of claims 1-10, further comprising an automated process control system configured to control to the system.~~

~~12.~~11. The system of any one of claims 1-1~~0~~1, further comprising a bed such that the blood withdrawal device and the cell therapy infusion device are collocated with the bed.

~~13.~~12. A cell therapy production system, comprising:

(a) a blood withdrawal device;

(b) an automated cell engineering system, including:

i. an enclosable housing;

ii. a cell separation device contained within the enclosable housing and fluidly connected to the blood withdrawal device;

iii. a cell transduction apparatus contained within the enclosable housing and fluidly connected to the cell separation device~~filter~~; and

iv. a cassette contained within the enclosable housing, the cassette comprising a low temperature chamber for storage of a cell culture media, and a high temperature chamber that includes a cell culture chamber fluidly connected to the cell transduction apparatus; ~~and~~

(c) an automated process control system configured to automatically control the cell therapy production system; and

(d) a cell therapy infusion device capable of returning the cell therapy to a patient, the cell therapy infusion device being fluidly connected to the cell culture chamber.

~~14.~~13. The system of claim 1~~2~~3, wherein the cell separation device is a cell separation filter includes a matrix which captures a T-cell population.

~~15.~~14. The system of claim 1~~2~~3 or claim 1~~3~~4, wherein the cell transduction apparatus is an electroporation unit.

~~16.~~15. The system of any one of claims 1~~2~~3-1~~4~~5, wherein the cassette further comprises one or more fluidics pathways, wherein the fluidics pathways provide recirculation, removal of waste and homogenous gas exchange and distribution of nutrients to the cell culture chamber without disturbing cells within the cell culture chamber.

~~17.~~16. The system of any one of claims 1~~2~~3-1~~5~~6, wherein the cassette further comprises one or more of a pH sensor, a glucose sensor, an oxygen sensor, a carbon dioxide sensor, and/or an optical density sensor.

~~18.~~17. The system of any one of claims 1~~2~~3-1~~6~~7, further comprising a computer control system and a user interface, wherein the user interface is coupled to the computer control system to provide instructions to the automated cell engineering system.

~~19.~~18. The system of any one of claims 1~~2~~3-1~~7~~8, wherein the system is portable.

~~20. The system of any one of claims 13-19, further comprising an automated process control system configured to control the system.~~

~~21.~~19. The system of any one of claims 1~~23~~-18~~20~~, further comprising a bed such that the blood withdrawal device and the cell therapy infusion device are collocated with the bed.

~~22. A method for preparing a cell therapy product, the method comprising:~~

~~(a) passing a blood sample withdrawn from a patient through a cell separation device to remove a target cell population from the blood sample;~~

~~(b) transducing the target cell population with a vector to produce a transduced cell culture;~~

~~(c) optionally expanding the transduced cell culture; and~~

~~(d) harvesting the cell culture;~~

~~wherein the harvested cell culture is to be infused into the patient.~~

~~23. The method of claim 22, wherein the cell separation device removes T-cells from the blood sample via a separation filter.~~

~~24. The method of claim 23, wherein the transducing comprises electroporating the T-cells with a vector including a chimeric antigen receptor.~~

~~25. The method of any one of claims 22-24, further comprising filtering, washing, and/or formulating the harvested cell culture, prior to the infusing.~~

~~26. The method any one of claims 22-25, wherein (a)-(f) are controlled by an automated process control system.~~