CLAIMS

1. A system for rejuvenating a cell culture medium, the system comprising:

(a) means for obtaining a cell culture medium essentially devoid of cells from at least one bioreactor using a cell retention device, wherein the cell culture medium comprises one or more waste molecules;

(b) means for separating charged molecules from the cell culture medium obtained from (a) using an electric field, thereby removing the one or more waste molecules from the cell culture medium and obtaining a rejuvenated medium essentially devoid of the one or more waste molecules;

(c) means for retaining uncharged molecules and macromolecules in the rejuvenated medium during separation and removal of the charged molecules; and

(d) means for circulating the rejuvenated medium back into the at least one bioreactor or at least one other bioreactor.

2. A system for rejuvenating a cell culture medium, the system comprising:

(a) means for obtaining a cell culture medium essentially devoid of cells from at least one bioreactor using a cell retention device, wherein the cell culture medium comprises one or more waste molecule;

(b) a nanofiltration means in fluid communication with the means in (a), wherein the nanofiltration means is operable to provide a filtered permeate reduced in the one or more waste molecules;

(c) means for separating charged molecules from the filtered permeate obtained from (b) using an electric field, thereby further reducing the one or more waste molecules from the cell culture medium and obtaining a rejuvenated medium essentially devoid of the one or more waste molecules;

(d) means for retaining uncharged molecules and macromolecules in the rejuvenated medium during separation and removal of the charged molecules; and

(e) means for circulating the rejuvenated medium back into the at least one bioreactor or into at least one other bioreactor.

3. A system for efficient growth of eucaryotic cells for medical or agriculture applications, the system comprising:

(a) at least one means for growing eucaryotic cells, such as a bioreactor, connected to a cell retention centrifuge, producing a waste medium essentially devoid of cells, wherein the waste medium is a cell culture medium comprising one or more waste molecules;

(b) means for collecting the waste medium and transferring the waste medium to a rejuvenation tank;

(c) a means for controlling the pH of the waste medium from (b) prior to nanofiltration and filtration;

(d) a means for nanofiltration of the waste medium from (b), thereby producing a permeate and a concentrated waste stream;

(e) a means of removal of one or more waste molecules, such as electrodialysis (ED), from the permeate, thereby producing a polished rejuvenation medium; and

(f) a means for recycling the concentrated waste stream and/or the polished rejuvenation medium back to the at least one means for growing eucaryotic cells, thereby increasing the efficient use of culture medium for eucaryotic cell growth.

4. The system of any one of claims 1 or 2, wherein the cell retention device comprises at least one hollow fiber with a pore cutoff between about 5 kD and about 5 microns, preferably about 3 microns.

5. The system of any one of claims 1-4, wherein the cell retention device or cell retention centrifuge comprises continuous centrifuge.

6. The system of any one of claims 1-4, wherein the cell retention device or cell retention centrifuge comprises dis-continuous centrifuge.

7. The system of claim 2, wherein the nanofiltration means has a molecular weight cutoff in the range of about 150 Da to about 300 Da.

8. The system of any one of claims 1 or 2, wherein the means for separating charged waste molecules from the cell culture medium comprises an electrodialysis unit.

9. The system of claim 8, wherein the electrodialysis unit comprises a bi-polar membrane which allows for separate recovery of lactic acid and ammonium.

10. The system of any one of claims 1 to 3, further comprising a conductivity sensor to measure the osmolarity of the rejuvenated medium.

11. Use of the system of any one of the preceding claims for production of cultured meat, glycosylated proteins, viruses, genetic materials, or vaccines.

12. A method for rejuvenating a cell culture medium, the method comprising:

(a) obtaining a cell culture medium essentially devoid of cells from at least one bioreactor using a cell retention device, wherein the cell culture medium comprises one or more waste molecules;

(b) separating charged molecules from the cell culture medium obtained from (a) using an electric field, thereby removing the one or more waste molecules from the cell culture medium and obtaining a rejuvenated medium essentially devoid of one or more waste molecules;

(c) retaining uncharged molecules and macromolecules in the rejuvenated medium during separation and removal of the one or more waste molecules; and

(d) circulating the rejuvenated medium back into the at least one bioreactor or at least one other reactor, thereby rejuvenating the cell culture medium.

13. A method for rejuvenating a cell culture medium, the method comprising:

(a) obtaining a cell culture medium essentially devoid of cells from at least one bioreactor using a cell retention device, wherein the cell culture medium comprises one or more waste molecules;

(b) passing the cell culture medium from (a) through a nanofiltration mean, wherein the nanofiltration means is operable to provide a filtered permeate reduced in the one or more waste molecules;

(c) separating charged molecules from the filtered permeate obtained from (b) using an electric field, thereby further reducing the one or more waste molecules from the cell culture medium and obtaining a rejuvenated medium essentially devoid of the one or more waste molecules;

(d) retaining uncharged molecules and macromolecules in the rejuvenated medium during separation and removal of the one or more waste molecules; and

(e) circulating the rejuvenated medium back into the at least one bioreactor or at least one other reactor, thereby rejuvenating the cell culture medium.

14. A method for efficient growth of eucaryotic cells for medical or agriculture applications, the method comprising:

(a) obtaining a cell culture medium essentially devoid of cells from at least one bioreactor using a cell retention centrifuge, thereby producing a waste medium essentially devoid of cells, wherein the waste medium is a cell culture medium comprising one or more waste molecules;

(b) collecting the waste medium and transferring the waste medium to a rejuvenation tank;

(c) controlling the pH of the waste medium from (b) prior to nanofiltration;

(d) passing the cell culture medium from (c) through a nanofiltration mean, thereby producing a permeate and a concentrated waste stream;

(e) removing one or more waste molecules from the permeate using an electric field, thereby producing a polished rejuvenated medium; and

(f) recycling the concentrated waste and/or the polished rejuvenated medium back to the at least one means for growing eucaryotic cells, thereby increasing the efficient use of culture medium for eucaryotic cell growth.

15. The method of any of claims 12-14, wherein the cell culture medium obtained from (a) further comprises one or more proteins.

16. The method of any one of claims 12-14, wherein the one or more waste molecules interfere with desired growth and/or desired differentiation of the cells, preferably wherein the one or more waste molecules include ammonia, ammonium, lactate, sodium, isovaleric acid, isobutyric acid,

2-methylbutyric acid, rosmarinic acid, 3-phenyllactic acid, DL-*p*-Hydroxyphenyllactic acid, fumarate, alanine, glutamic acid, aspartic acid, reactive oxygen and nitrogen species, or a combination thereof, preferably ammonia, ammonium, and/or lactate.

17. The method of any one of claims 12-16, wherein the rejuvenated medium contains one or more proteins selected from the group consisting of albumin, catalase, insulin, fibroblast growth factor, transforming growth factor beta, and super oxide dismutase.

18. The method of any one of claims 12-14, wherein the cell retention device or cell retention centrifuge comprises continuous or non-continuous centrifuge, wherein the centrifuge preferably operates at 300 to 20,000×g, more preferably at 500×g, thereby removing cells from the cell culture medium and creating a waste medium devoid of cells for rejuvenation.

19. The method of any one of claims 12-14, wherein the electric field is provided by an electrodialysis unit, preferably employing a voltage in the range of about 5-30 volts on the cell culture medium.

20. The method of any one of the claim 12-14, wherein the cell culture medium has been adjusted to a pH value in the range of about 6-8, preferably about 7.

21. The method of any one of claims 12-20, wherein the rejuvenated medium comprising salts and metals is further processed at a pH in the range of about 6-8 and wherein the rejuvenated medium comprises iron and zinc adjusted to at least 0.05 mg/L before returning to the bioreactor.

22. The method of any one of claim 12-21, wherein the osmolarity of the rejuvenated medium is about 280-320 milliosmoles per kilogram (mOsm/kg) before returning to the bioreactor.

23. The method of any one of claims 12-22, wherein the rejuvenated cell culture medium is used for production of cultured meat, glycosylated proteins, viruses, genetic materials, or vaccines.

24. A method for expanding cells in a bioreactor, said method comprising:

(a) culturing cells in a cell culture medium comprising nutrients and waste molecules; and

(b) rejuvenating the cell culture medium according to the method of any one of claims 12 to 23 to reduce the amount of the one or more waste molecules or remove the one or more waste molecules from the cell culture medium.

25. The method of claim 24, wherein the expanded cells are used to produce cultured meat, glycosylated proteins, viruses, genetic materials, or vaccines.