AU 2020 210244 A1 and CA 2190628 C teach devices for implantation of insulin producing cells, having large pores with a diameter in the range of 0.4 µm, and an inner diameter of more than 1.5 mm. WO 1997/013474 A1 discloses a flat sheet type device for implantation into a mammalian host, in which cells producing insulin are embedded in alginate and the admixture is further covered with another alginate layer. WO 2014/202199 A1 also teaches a device for implantation comprising a dialysis tube with pores in the range of from 40 to 290 µm.

Nonetheless, the solutions provided by the prior art were not optimal under at least one of the aforesaid desirable aspects, in particular productivity over extended periods of time and having an option to replace cells in case production of the therapeutic compound decreases below the desirable level. Thus, there is a need for improved means and methods for implanting cells producing therapeutic compounds into a mammalian host, avoiding at least in part the drawbacks of the prior art. This problem is solved by the means and methods of the present invention, with the features of the independent claims. Preferred embodiments, which might be realized in an isolated fashion or in any arbitrary combination are listed in the dependent claims.

In ~~accordance~~one aspect, the present ~~invention~~ disclosure relates to a device for implantation into a mammalian host, said device comprising

a) a dialysis tube with a lumen and a dialysis membrane enclosing said lumen, wherein

(i) the dialysis tube has an outer diameter of from 20 µm to 600 µm; and

(ii) the dialysis membrane has a molecular weight cutoff of from 25 kDa to 150 kDa and comprises at least one material selected from the group consisting of polyethersulfone, polyarylethersulfone, polyethylene, polytetrafluoroethylene, polyvinylidene fluoride, and polypropylene; and

b) a therapeutic composition disposed within the lumen of the dialysis tube, wherein said therapeutic composition comprises a plurality of cells secreting a therapeutic compound and a matrix material embedding said cells secreting a therapeutic compound, wherein the matrix material is selected from alginate, collagen, fibrin, extracellular matrix material, synthetic hydrogel, and acrylate.~~,~~ ~~in~~In an ~~embodiment~~ example the matrix material is alginate.

In another aspect, the present disclosure relates to a method of producing a device for implantation as described herein comprising:

a) filling the dialysis tube with a plurality of cells secreting a therapeutic compound and a matrix material;

b) at least temporarily sealing at least one end of the dialysis tube; and

c) thereby, producing a device for implantation.

In another aspect, the present disclosure relates to a port system, comprising:

I) a device for implantation comprising a port as described herein and/or a device for implantation obtained or obtainable as described herein; and

II) an extracorporal connecting head.

In another aspect, the present disclosure relates to a cell secreting a therapeutic compound for use in treating disease by implantation of said cell in a device for implantation as described herein and/or obtained or obtainable according to the method as described herein.

In another aspect, the present disclosure relates to a cell secreting a therapeutic compound for use in treating diabetes, Hemophilia B, huGH deficiency, osteoporosis, Parkinson´s disease, acromegaly, an endocrine tumor, alpha1-antitrypsin -deficiency, an infectious disease, an autoimmune disease, cancer, or chronic virus infection by implantation of said cell in a device for implantation as described herein and/or obtained or obtainable according to the method as described herein.

In general, terms used herein are to be given their ordinary and customary meaning to a person of ordinary skill in the art and, unless indicated otherwise, are not to be limited to a special or customized meaning. As used in the following, the terms “have”, “comprise” or “include” or

Claims

1. A device for implantation ~~(10)~~ into a mammalian host, said device ~~(10)~~ comprising
a) a dialysis tube ~~(20)~~ with a lumen ~~(30)~~ and a dialysis membrane ~~(40)~~ enclosing said lumen ~~(30)~~, wherein
i) the dialysis tube ~~(20)~~ has an outer diameter of from 20 µm to 600 µm; and
ii) the dialysis membrane ~~(40)~~ has a molecular weight cutoff of from 25 kDa to 150 kDa and comprises at least one material selected from the group consisting of polyethersulfone, polyarylethersulfone, polyethylene, polytetrafluoroethylene, polyvinylidene fluoride, and polypropylene; and
b) a therapeutic composition disposed within the lumen ~~(30)~~ of the dialysis tube ~~(20)~~, wherein said therapeutic composition comprises a plurality of cells secreting a therapeutic compound ~~(50)~~ and a matrix material ~~(60)~~ embedding said cells secreting a therapeutic compound ~~(50)~~, wherein the matrix material ~~(60)~~ is selected from alginate, collagen, fibrin, extracellular matrix material, synthetic hydrogel, and acrylate.

2. The device ~~(10)~~ of claim 1, wherein the dialysis tube ~~(20)~~ has an outer diameter of from 400 µm to 500 µm.

3. The device ~~(10)~~ of claim 1 or 2, wherein the dialysis membrane ~~(40)~~ has a molecular weight cutoff of from 80 kDa to 100 kDa.

4. The device ~~(10)~~ of any one of claims 1 to 3, wherein said device ~~(10)~~ further comprises an implantable first guiding system ~~(140)~~ at least partially guiding the dialysis tube ~~(20)~~ through a subcutaneous tissue.

5. The device ~~(10)~~ of any one of claims 1 to 4, wherein said device ~~(10)~~ further comprises a port ~~(70)~~ providing access to the dialysis tubing ~~(20)~~ from the bodily surface of the mammalian host and/or from a subcutaneous access element.

6. The device ~~(10)~~ of claim 5, wherein said port ~~(70)~~ is a transcutaneously implantable port.

7. The device ~~(10)~~ of claim 5 or 6, wherein said port ~~(70)~~ comprises a fixing element ~~(80)~~ fixing the port ~~(70)~~ within or under the skin of the mammalian host.

8. The device ~~(10)~~ of any one of claims 1 to 7, wherein at least the dialysis tube ~~(20)~~ of the device ~~(10)~~ is at least partially implanted intraperitoneally, subcutaneously, intraarterially, or intravenously.

9. The device ~~(10)~~ of any one of claims 1 to 8, wherein said device ~~(10)~~ is adapted for in situ replacement of said dialysis tube ~~(20)~~ and/or for in situ replacement of the content of the dialysis tube ~~(20)~~.

10. The device ~~(10)~~ of any one of claims 1 to 9, wherein the therapeutic compound is selected from the group consisting of insulin, glucagon, Factor IX, human growth hormone (huGH), Calcitonin, Glucagon-like peptide (GLP-1) and agonists, Amylin, levodopa, somatostatin, alpha1-antitrypsin (AAT), interleukins, and interferons.

11. The device ~~(10)~~ of any one of claims 1 to 10, wherein the therapeutic compound is insulin or an insulin analog, wherein the plurality of cells secreting a therapeutic compound ~~(50)~~ is adapted to secrete an amount of insulin and wherein the secreted amount of insulin is related to the concentration of glucose present in the matrix material.

12. A method of producing a device ~~(10)~~ for implantation according to any one of claims 1 to 11 comprising:
    a) filling the dialysis tube ~~(20)~~ with a plurality of cells secreting a therapeutic compound ~~(50)~~ and a matrix material ~~(60)~~;
    b) at least temporarily sealing at least one end of the dialysis tube ~~(20)~~; and
    c) thereby, producing a device for implantation ~~(10)~~.

13. A port system ~~(200)~~, comprising:
    I) a device for implantation ~~(10)~~ comprising a port ~~(70)~~ according to any one of claims 5 to 11 and/or a device for implantation ~~(10)~~ obtained or obtainable according to claim 12; and
    II) an extracorporal connecting head ~~(160)~~.

14. A cell secreting a therapeutic compound ~~(50)~~ for use in treating disease by implantation of said cell in a device for implantation ~~(10)~~ according to any one of claims 1 to 11 and/or obtained or obtainable according to the method according to claim 12.

15. A cell secreting a therapeutic compound ~~(50)~~ for use in treating diabetes, Hemophilia B, huGH deficiency, osteoporosis, Parkinson´s disease, acromegaly, an endocrine tumor, alpha1-antitrypsin -deficiency, an infectious disease, an autoimmune disease, cancer, or chronic virus infection by implantation of said cell in a device for implantation ~~(10)~~ according to any one of claims 1 to 11 and/or obtained or obtainable according to the method according to claim 12.