

Claims

1. Use of normal cells taken from an internal organ of a subject in the manufacture of a medicament for the treatment of a diseased or dysfunctional internal organ wherein the medicament is formed by the following steps:

- a. obtaining normal cells of an internal organ from a donor;
 - b. combining the cells with one or more gel-forming biomaterials to form a mixture;
- and

c. optionally, combining the mixture with nutrient medium, signaling molecules, extracellular matrix proteins, or a combination thereof;

wherein the resulting medicament formed from step b or step c is to be introduced into the subject in such a manner that a substantial portion of the cells take up residence in or on at least a portion of the internal organ *in vivo*.

2. Normal internal organ cells for use in the treatment of the internal organ, wherein the cells are first:

- a. obtained from a donor;
- b. combined with one or more gel-forming biomaterials to form a mixture; and
- c. optionally, combining the mixture with nutrient medium, signaling molecules, extracellular matrix proteins, or a combination thereof;

whereby the resulting mixture formed from step b or step c is to be introduced into the subject in such a manner that a substantial portion of the cells take up residence in or on at least a portion of the internal organ *in vivo*.

3. The use according to claim 1 or the normal cells according to claim 2, in which the normal cells are stem cells, committed progenitors, or mature cells.

4. The use according to claim 1 or the normal cells according to claim 2, in which the internal organ is liver, lung, gut, intestine, heart, kidney, biliary tree, thyroid, thymus, thyroid, brain, or pancreas.

5. The use according to claim 3 or the normal cells according to claim 3, in which the internal organ is liver.

6. The use according to claim 3 or the normal cells according to claim 3, in which the suspension of cells are liver stem cells, hepatoblasts, committed progenitors of biliary epithelia or hepatocytes, or mature hepatocytes or cholangiocytes.
7. The use according to claim 1 or the normal cells according to claim 2, in which the donor is the subject having the internal organ in diseased or dysfunctional condition and the normal cells are obtained from a portion of the internal organ that is not diseased or dysfunctional.
8. The use according to claim 1 or the normal cells according to claim 2, in which the donor is a non-autologous donor.
9. The use according to claim 1 or the normal cells according to claim 2, in which the donor is a foetus, a neonate, a child, or an adult.
10. The use according to claim 1 or the normal cells according to claim 2, in which the additional cells comprise angioblasts, endothelial cells, stellate cell precursors, stellate cells, stromal cells, epithelial stem cells, mature parenchymal cells or combinations thereof.
11. The use according to claim 1 or the normal cells according to claim 2, in which the one or more biomaterials comprise collagens, laminins, adhesion molecules, proteoglycans, hyaluronans, glycosaminoglycan chains, chitosan, alginate, and synthetic, biodegradable and biocompatible polymers, or combinations thereof.
12. The use according to claim 1 or the normal cells according to claim 2, in which the signaling molecules comprise fibroblast growth factor, hepatocyte growth factor, epidermal growth factor, vascular endothelial cell growth factor (VEGF), insulin like growth factor I, insulin-like growth factor II (IGF-II), oncostatin-M, leukemia inhibitory factor (LIF), interleukins, transforming growth factor- β (TGF- β), HGF, transferrin, insulin, transferrin/fe, tri-iodothyronine, T3, glucagon, gluco-corticoids, growth hormones, estrogens, androgens, thyroid hormones, and combinations thereof.
13. The use according to claim 12 or the normal cells according to claim 12, in which the interleukins are/ IL-6, IL-11, IL-13, or combinations thereof.

14. The use according to claim 1 or the normal cells according to claim 2, in which the cells are cultured in serum-free medium.

15. The use according to claim 14 or the normal cells according to claim 14, in which the medium comprises insulin, transferrin, lipids, calcium, zinc and selenium.

16. The use according to claim 1 or the normal cells according to claim 2, in which the suspension of cells of the internal organ are solidified *ex vivo* within the biomaterials prior to introducing the cells into the subject.

17. The use according to claim 1 or the normal cells according to claim 2, in which the suspension of cells is introduced to or in the proximity of the diseased or dysfunctional tissue.

18. The use according to claim 17 or the normal cells according to claim 17, in which the suspension of cells is introduced directly into a tissue.

19. The use according to claim 18 or the normal cells according to claim 18, in which the tissue is omentum or liver.

20. The use according to claim 1 or the normal cells according to claim 2, in which the suspension of cells is to be introduced via injection, biodegradable covering, or sponge.

21. A method of cryopreserving cells, comprising:

- a. obtaining cells to be transplanted;
- b. combining the cells with gel-forming biomaterials to form a mixture;
- c. optionally combining the mixture with one or more of isotonic nutrient medium, signaling molecules and extracellular matrix components;
- d. freezing the mixture.

22. The use according to claim 1 or the normal cells according to claim 2, in which the one or more biomaterials comprise collagens, laminins, adhesion molecules, proteoglycans,

hyaluronans, glycosaminoglycan chains, chitosan, alginate, and synthetic, biodegradable and biocompatible polymers, or combinations thereof.

23. The use according to claim 22 or the normal cells according to claim 22, in which the biomaterial comprises hyaluronans.

24. The method according to claim 21, in which the cell suspension is further combined with a cryoprotectant selected from the group consisting of dimethyl sulfoxide(DMSO), glycerol, ethylene glycol, ethaediol, 1,2-propaendiol, 2, 3-butenediol, formamide, N-methylformamide, 3-methoxy-1,2-propanediol by themselves, and combinations thereof.

25. The method according to claim 21, in which the cell suspension is further combined with a sugar, glycine, alanine, polyvinylpyrrolidone, pyruvate, an apoptosis inhibitor, calcium, lactobionate, raffinose, dexamethasone, reduced sodium ions, choline, antioxidants, hormones, or combination thereof.

26. The method according to claim 25, in which the sugar is trehalose, fructose, glucose, or a combination thereof.

27. The method according to claim 25, in which the antioxidants are vitamin E, vitamin A, beta-carotene, or a combination thereof.

28. A tissue graft comprising cells admixed with one or more biomaterials to form a graft, wherein the components of the graft have a shear moduli ranging from 25 to 520 Pa.

29. A graft composition capable of localizing cells of an internal organ onto a surface, into an interior portion, or both of a target internal organ comprising cells of an internal organ and a solution of one or more hydrogel-forming precursors, in the presence of an effective amount of a cross-linker, wherein the graft composition may be applied onto a surface, into an interior portion, or both of a target internal organ *in vivo*, and wherein the graft composition forms a hydrogel comprising cells of an internal organ on a surface, in an interior portion, or both of a target internal organ.

30. The graft composition of claim 29 in which cells of an internal organ are localized for a period of at least twelve hours, at least twenty-four hours, or at least about forty-eight hours

or at least seventy-two hours, onto a surface, into an interior portion, or both of a target internal organ.

31. The graft composition of claim 29 in which the cells of an internal organ are not tumor or cancer cells or diseased cells.

32. The graft composition of claim 29 in which the cells of an internal organ are normal cells, tumor or cancer cells, or cells infected with a pathogen selected from the group consisting of virus, bacteria, malaria.

33. The graft composition of claim 29 in which the one or more hydrogel-forming precursors comprise glycosaminoglycans, hyaluronans, proteoglycand, gelatins, collagens, laminins, other attachment proteins, plant-derived matrix components, denatured forms thereof, or combinations thereof.

34. The graft composition of claim 29 in which the one or more hydrogel-forming precursors are comprised of a thiol-modified sodium hyaluronate and a thiol-modified gelatin.

35. The graft compoition of claim 29 in which the cross-linker comprises polyethylene glycol di-acrylate or a disulfide-containing derivative thereof.

36. The graft composition of claim 29 in which the hydrogel possesses a viscosity ranging from about 0.1 to about 100 kPa, preferably about 1 to about 10 kPa, more preferably about 2 to about 4 kPa.

37. The graft composition of claim 29 in which the graft composition, in the presence of an effective amount of a cross-linker, may be introduced into a pocket formed on a surface of a target internal organ.

38. The graft composition of claim 37 in which the pocket if prepared from omentum, spider silk, and/or insect silk.

39. The graft composition of claim 29 in which the target internal organ is selected from the group consisting of liver, pancreas, biliary tree, thyroid, intestine, lung, prostate, breast, brain, uterus, bone, or kidney.

40. The graft composition of claim 29 in which the hydrogel forms *in situ*.