Claims

1. A bioartificial proximal tubule device comprising a decellularized biological matrix scaffold seeded with one or more precursor cells under conditions sufficient to allow the differentiation of the precursor cell into renal proximal tubule epithelial cells without the use of a MEK inhibitor, wherein the differentiated cells form an epithelial monolayer on the scaffold, and wherein the one or more precursor cells is selected from the group consisting of primary renal tubule epithelial cells, inducible pluripotent stem cells differentiated into renal cells or renal progenitor cells, progenitor cells differentiated into renal cells or renal progenitor cells, stem cells isolated from the kidney or progenitor cells isolated from the kidney, and mixtures thereof.

2. A bioartificial proximal tubule device comprising a decellularized biological scaffold having at least two surfaces wherein at least one surface is seeded with one or more precursor cells under conditions sufficient to allow differentiation of the cells into renal proximal tubule epithelial cells, wherein the cells form an epithelial monolayer on the surface of the scaffold without the use of a MEK inhibitor, and wherein the one or more precursor cells is selected from the group consisting of primary renal tubule epithelial cells, inducible pluripotent stem cells differentiated into renal cells or renal progenitor cells, progenitor cells differentiated into renal cells or renal progenitor cells, stem cells isolated from the kidney or progenitor cells isolated from the kidney, and mixtures thereof.

3. The bioartificial proximal tubule device of claims 1 or 2, wherein the decellularized biological matrix scaffold is derived from mammalian tissue.

4. The bioartificial proximal tubule device of claim 3, wherein the decellularized biological matrix scaffold is derived from mucosal or submucosal tissue.

5. The bioartificial proximal tubule device of claim 3, wherein the decellularized biological matrix scaffold is derived from a mammalian alimentary canal.

6. The bioartificial proximal tubule device of claim 5, wherein the decellularized biological matrix scaffold is derived from the stomach, duodenum, jejunum, ileum or colon of a mammal.

7. The bioartificial proximal tubule device of any of claims 1 to 6, wherein the progenitor cells are human kidney-derived cells.

8. The bioartificial proximal tubule device of claim 7, wherein the human kidney-derived cells are capable of self-renewal and expansion in culture and are positive for expression of at least one of Oct-4, Rex-1, Pax-2, Cadherin-11, FoxD1, WT1, Eya1, HNF3B, CXC-R4, Sox-17, EpoR, BMP2, BMP7, or GDF5; and negative for the expression of at least one of Sox2, FGF4, hTert, Wnt-4, SIX2, E-cadherin or GATA-4.

9. The bioartificial proximal tubule device of claims 7 or 8, wherein the human kidney-derived cells are positive for at least one of cell-surface markers HLA-I, CD24, CD29, CD44, CD49c, CD73, CD90, CD166, or SSEA-4; and negative for at least one of cell-surface markers HLA II, CD31, CD34, CD45, CD56, CD80, CD86, CD104, CD105, CD117, CD133, CD138, and CD141.

10. The bioartificial proximal tubule device of any of claims 7 to 9, wherein the human kidney-derived cells secrete at least one of trophic factors FGF2, HGF, TGFα, TIMP-1, TIMP-2, MMP-2 or VEGF; and do not secrete at least one of trophic factors PDGF-bb or IL12p70.

11. The bioartificial proximal tubule device of claim 7, wherein the human kidney-derived cells capable of self-renewal and expansion in culture and positive for expression of HLA-I and at least one of Oct-4, Rex-1, Pax-2, Cadherin-11, FoxD1, WT1, Eya1, HNF3B, CXC-R4, Sox-17, EpoR, BMP2, BMP7, or GDF5; and negative for the expression of CD133 and at least one of Sox2, FGF4, hTert, Wnt-4, SIX2, E-cadherin or GATA-4.

12. A method of differentiating one or more precursor cells into renal cells comprising seeding a decellularized biological matrix scaffold with one or more precursor cells and culturing the cells on the scaffold under conditions sufficient to allow the differentiation of the precursor cell into renal proximal tubule epithelial cells, wherein the differentiated cells form an epithelial monolayer on the scaffold, wherein the method does not comprise use of a MEK inhibitor, and wherein the one or more precursor cells is selected from the group consisting of primary renal tubule epithelial cells, inducible pluripotent stem cells differentiated into renal cells or renal

progenitor cells, progenitor cells differentiated into renal cells or renal progenitor cells, stem cells isolated from the kidney or progenitor cells isolated from the kidney, and mixtures thereof.

13. The method of claim 12, wherein the decellularized biological matrix scaffold is derived from mammalian tissue.

14. The method of claim 13, wherein the decellularized biological matrix scaffold is derived from mucosal or submucosal tissue.

15. The method of claim 12, wherein the decellularized biological matrix scaffold is derived from the stomach, duodenum, jejunum, ileum or colon of a mammal.

16. The method of claims 12 to 15, wherein the progenitor cells are human kidney-derived cells.

17. The method of claim 16, wherein the human kidney-derived cells are capable of self-renewal and expansion in culture and are positive for expression of at least one of Oct-4, Rex-1, Pax-2, Cadherin-11, FoxD1, WT1, Eya1, HNF3B, CXC-R4, Sox-17, EpoR, BMP2, BMP7, or GDF5; and negative for the expression of at least one of Sox2, FGF4, hTert, Wnt-4, SIX2, E-cadherin or GATA-4.

18. The method of claim 17, wherein the human kidney-derived cells are positive for at least one of cell-surface markers HLA-I, CD24, CD29, CD44, CD49c, CD73, CD90, CD166, or SSEA-4; and negative for at least one of cell-surface markers HLA II, CD31, CD34, CD45, CD56, CD80, CD86, CD104, CD105, CD117, CD133, CD138, and CD141.

19. The method of claim 18, wherein the human kidney-derived cells secrete at least one of trophic factors FGF2, HGF, TGFα, TIMP-1, TIMP-2, MMP-2 or VEGF; and do not secrete at least one of trophic factors PDGF-bb or IL12p70.

20. The bioartificial proximal tubule device of any of claims 1 to 6 or 7 to 11, wherein the epithelial monolayer is stable.

21. The bioartificial proximal tubule device of any of claims 1 to 6 or 7 to 11, wherein the differentiated cells maintain contact inhibition.

22. The method of any claims 12 to 15 and 16 to 18, wherein the epithelial monolayer is stable.

23. The method of any claims 12 to 15 and 16 to 18, wherein the differentiated cells maintain contact inhibition.

Claims

1. A bioartificial proximal tubule device comprising a decellularized biological matrix scaffold seeded with one or more precursor cells under conditions sufficient to allow the differentiation of the precursor cell into renal proximal tubule epithelial cells without the use of a MEK inhibitor, wherein the differentiated cells form an epithelial monolayer on the scaffold, and wherein the one or more precursor cells is selected from the group consisting of primary renal tubule epithelial cells, inducible pluripotent stem cells differentiated into renal cells or renal progenitor cells, progenitor cells differentiated into renal cells or renal progenitor cells, stem cells isolated from the kidney or progenitor cells isolated from the kidney, and mixtures thereof.

2. A bioartificial proximal tubule device comprising a decellularized biological scaffold having at least two surfaces wherein at least one surface is seeded with one or more precursor cells under conditions sufficient to allow differentiation of the cells into renal proximal tubule epithelial cells, wherein the cells form an epithelial monolayer on the surface of the scaffold without the use of a MEK inhibitor, and wherein the one or more precursor cells is selected from the group consisting of primary renal tubule epithelial cells, inducible pluripotent stem cells differentiated into renal cells or renal progenitor cells, progenitor cells differentiated into renal cells or renal progenitor cells, stem cells isolated from the kidney or progenitor cells isolated from the kidney, and mixtures thereof.

3. The bioartificial proximal tubule device of claims 1 or 2, wherein the decellularized biological matrix scaffold is derived from mammalian tissue.

4. The bioartificial proximal tubule device of claim 3, wherein the decellularized biological matrix scaffold is derived from mucosal or submucosal tissue.

5. The bioartificial proximal tubule device of claim 3, wherein the decellularized biological matrix scaffold is derived from a mammalian alimentary canal.

6. The bioartificial proximal tubule device of claim 5, wherein the decellularized biological matrix scaffold is derived from the stomach, duodenum, jejunum, ileum or colon of a mammal.

7. The bioartificial proximal tubule device of any of claims 1 to 6, wherein the progenitor cells are human kidney-derived cells.

8. The bioartificial proximal tubule device of claim 7, wherein the human kidney-derived cells are capable of self-renewal and expansion in culture and are positive for expression of at least one of Oct-4, Rex-1, Pax-2, Cadherin-11, FoxD1, WT1, Eya1, HNF3B, CXC-R4, Sox-17, EpoR, BMP2, BMP7, or GDF5; and negative for the expression of at least one of Sox2, FGF4, hTert, Wnt-4, SIX2, E-cadherin or GATA-4.

9. The bioartificial proximal tubule device of claims 7 or 8, wherein the human kidney-derived cells are positive for at least one of cell-surface markers HLA-I, CD24, CD29, CD44, CD49c, CD73, CD90, CD166, or SSEA-4; and negative for at least one of cell-surface markers HLA II, CD31, CD34, CD45, CD56, CD80, CD86, CD104, CD105, CD117, CD133, CD138, and CD141.

10. The bioartificial proximal tubule device of any of claims 7 to 9, wherein the human kidney-derived cells secrete at least one of trophic factors FGF2, HGF, TGFα, TIMP-1, TIMP-2, MMP-2 or VEGF; and do not secrete at least one of trophic factors PDGF-bb or IL12p70.

11. The bioartificial proximal tubule device of claim 7, wherein the human kidney-derived cells capable of self-renewal and expansion in culture and positive for expression of HLA-I and at least one of Oct-4, Rex-1, Pax-2, Cadherin-11, FoxD1, WT1, Eya1, HNF3B, CXC-R4, Sox-17, EpoR, BMP2, BMP7, or GDF5; and negative for the expression of CD133 and at least one of Sox2, FGF4, hTert, Wnt-4, SIX2, E-cadherin or GATA-4.

12. A method of differentiating one or more precursor cells into renal cells comprising seeding a decellularized biological matrix scaffold with one or more precursor cells and culturing the cells on the scaffold under conditions sufficient to allow the differentiation of the precursor cell into renal proximal tubule epithelial cells, wherein the differentiated cells form an epithelial monolayer on the scaffold, wherein the method does not comprise use of a MEK inhibitor, and wherein the one or more precursor cells is selected from the group consisting of primary renal tubule epithelial cells, inducible pluripotent stem cells differentiated into renal cells or renal

progenitor cells, progenitor cells differentiated into renal cells or renal progenitor cells, stem cells isolated from the kidney or progenitor cells isolated from the kidney, and mixtures thereof.

13. The method of claim 12, wherein the decellularized biological matrix scaffold is derived from mammalian tissue.

14. The method of claim 13, wherein the decellularized biological matrix scaffold is derived from mucosal or submucosal tissue.

15. The method of claim 12, wherein the decellularized biological matrix scaffold is derived from the stomach, duodenum, jejunum, ileum or colon of a mammal.

16. The method of claims 12 to 15, wherein the progenitor cells are human kidney-derived cells.

17. The method of claim 16, wherein the human kidney-derived cells are capable of self-renewal and expansion in culture and are positive for expression of at least one of Oct-4, Rex-1, Pax-2, Cadherin-11, FoxD1, WT1, Eya1, HNF3B, CXC-R4, Sox-17, EpoR, BMP2, BMP7, or GDF5; and negative for the expression of at least one of Sox2, FGF4, hTert, Wnt-4, SIX2, E-cadherin or GATA-4.

18. The method of claim 17, wherein the human kidney-derived cells are positive for at least one of cell-surface markers HLA-I, CD24, CD29, CD44, CD49c, CD73, CD90, CD166, or SSEA-4; and negative for at least one of cell-surface markers HLA II, CD31, CD34, CD45, CD56, CD80, CD86, CD104, CD105, CD117, CD133, CD138, and CD141.

19. The method of claim 18, wherein the human kidney-derived cells secrete at least one of trophic factors FGF2, HGF, TGFα, TIMP-1, TIMP-2, MMP-2 or VEGF; and do not secrete at least one of trophic factors PDGF-bb or IL12p70.

20. The bioartificial proximal tubule device of any of claims 1 to 11, wherein the epithelial monolayer is stable.

21. The bioartificial proximal tubule device of any of claims 1 to 11, wherein the differentiated cells maintain contact inhibition.

22. The method of any claims 12 to 18, wherein the epithelial monolayer is stable.

23. The method of any claims 12 to 18, wherein the differentiated cells maintain contact inhibition.