

Claims

What is claimed is:

1. Use of an organ from a donor swine in the manufacture of a medicament for xenotransplantation, wherein the manufacture comprises cross-dressing the organ with human CD47 by exposure to cells expressing human CD47 or extracellular vesicles (EVs) comprising human CD47; and wherein the cross-dressed organ is to be transplanted into a human recipient.
2. The use of claim 1, wherein the cross-dressing step comprises exposing the organ to human CD47 comprising extracellular vesicles (EVs).
3. The use of claim 2, wherein the EVs are isolated from human cells.
4. The use of claim 3, wherein the cells express recombinant human CD47.
5. The use of claim 3 or 4, wherein the cells are transgenic cells.
6. The use of any one of claims 2 to 5, wherein the cross-dressing is achieved by incubating the organ with EVs expressing human CD47 for 2 hours.
7. The use of any one of claims 2 to 5, wherein the cross-dressing is achieved by incubating the organ with EVs expressing human CD47 for 6 hours.
8. The use of any one of claims 2 to 5, wherein the cross-dressing is achieved by *ex vivo* perfusing the organ.
9. The use of any one of claims 1 to 8, wherein the use results in decreased phagocytosis by human macrophages.
10. The use of any one of claims 1 to 8, wherein the use results in decreased phagocytosis of the cross-dressed organ cells by human macrophages by 5% to 25% compared to non-cross-dressed organ cells as measured by FACS analysis of the percentage of CD14-positive cells engulfing cross-dressed cells.
11. The use of any one of claims 1 to 8, wherein the use results in decreased phagocytosis of the cross-dressed organ cells by human macrophages by 25% to 50% compared

to non-cross-dressed organ cells as measured by FACS analysis of the percentage of CD14-positive cells engulfing cross-dressed cells.

12. The use of any one of claims 1 to 8, wherein the use results in decreased phagocytosis of the cross-dressed organ cells by human macrophages by 50% to 75% compared to non-cross-dressed organ cells as measured by FACS analysis of the percentage of CD14-positive cells engulfing cross-dressed cells.

13. The use of any one of claims 1 to 8, wherein the use results in decreased phagocytosis of the cross-dressed organ cells by human macrophages by 75% to 80% compared to non-cross-dressed organ cells as measured by FACS analysis of the percentage of CD14-positive cells engulfing cross-dressed cells.

14. The use of any one of claims 1 to 8, wherein the use results in decreased phagocytosis of the cross-dressed organ cells by human macrophages by 80% to 85% compared to non-cross-dressed organ cells as measured by FACS analysis of the percentage of CD14-positive cells engulfing cross-dressed cells.

15. The use of any one of claims 1 to 8, wherein the use results in decreased phagocytosis of the cross-dressed organ cells by human macrophages by 85% to 90% compared to non-cross-dressed organ cells as measured by FACS analysis of the percentage of CD14-positive cells engulfing cross-dressed cells.

16. The use of any one of claims 1 to 8, wherein the use results in decreased phagocytosis of the cross-dressed organ cells by human macrophages by 90% to 95% compared to non-cross-dressed organ cells as measured by FACS analysis of the percentage of CD14-positive cells engulfing cross-dressed cells.

17. The use of any one of claims 1 to 8, wherein the use results in no detectable phagocytosis of the cross-dressed organ as measured by FACS analysis of the percentage of CD14-positive cells engulfing cross-dressed cells.

18. The use of any one of claims 1 to 8, wherein the use results in increased viability of the organ by protection from human macrophages as measured by FACS analysis of the percentage of CD14-positive cells engulfing cross-dressed cells.

19. The use of any one of claims 1 to 18, wherein the cross-dressed organ evades phagocytosis without induction of apoptosis.

20. The use of any one of claims 1 to 18, wherein the cross-dressed organ evades phagocytosis and does not exhibit any detectable level of apoptosis.

21. The use of any one of claims 1 to 18, wherein cells obtained from the cross-dressed organ exhibit 5% to 25% lower levels of apoptosis compared to cells obtained from a non-cross-dressed organ.

22. The use of any one of claims 1 to 18, wherein cells obtained from the cross-dressed organ exhibit 25% to 50% lower levels of apoptosis compared to cells obtained from a non-cross-dressed organ.

23. The use of any one of claims 1 to 18, wherein cells obtained from the cross-dressed organ exhibit 50% to 75% lower levels of apoptosis compared to cells obtained from a non-cross-dressed organ.

24. The use of any one of claims 1 to 18, wherein cells obtained from the cross-dressed organ exhibit 75% to 80% lower levels of apoptosis compared to cells obtained from a non-cross-dressed organ.

25. The use of any one of claims 1 to 18, wherein cells obtained from the cross-dressed organ exhibit 80% to 85% lower levels of apoptosis compared to cells obtained from a non-cross-dressed organ.

26. The use of any one of claims 1 to 18, wherein cells obtained from the cross-dressed organ exhibit 85% to 90% lower levels of apoptosis compared to cells obtained from a non-cross-dressed organ.

27. The use of any one of claims 1 to 18, wherein cells obtained from the cross-dressed organ exhibit at least 90% lower levels of apoptosis compared to cells obtained from a non-cross-dressed organ.

28. The use of any one of claims 19 to 27, wherein apoptosis is measured by propidium iodide staining.

29. The use of any one of claims 1 to 28, wherein the cross-dressed organ exhibits reduced inflammation, compared to a non-cross-dressed organ.

30. The use of any one of claims 1 to 28, wherein the cross-dressed organ exhibits 5% to 25% reduced inflammation, compared to a non-cross-dressed organ.

31. The use of any one of claims 1 to 28, wherein the cross-dressed organ exhibits 25% to 50% reduced inflammation, compared to a non-cross-dressed organ.

32. The use of any one of claims 1 to 28, wherein the cross-dressed organ exhibits 50% to 75% reduced inflammation, compared to a non-cross-dressed organ.

33. The use of any one of claims 1 to 28, wherein the cross-dressed organ exhibits 75% to 80% reduced inflammation, compared to a non-cross-dressed organ.

34. The use of any one of claims 1 to 28, wherein the cross-dressed organ exhibits 80% to 85% reduced inflammation, compared to a non-cross-dressed organ.

35. The use of any one of claims 1 to 28, wherein the cross-dressed organ exhibits 85% to 90% reduced inflammation, compared to a non-cross-dressed organ.

36. The use of any one of claims 1 to 28, wherein the cross-dressed organ exhibits at least 90% reduced inflammation, compared to a non-cross-dressed organ.

37. The use of any one of claims 1 to 36, wherein the human recipient exhibits reduced systemic inflammation post transplantation, compared to transplantation with a non-cross-dressed organ.

38. The use of any one of claims 1 to 36, wherein the human recipient exhibits 5% to 25% reduced systemic inflammation post transplantation, compared to transplantation with a non-cross-dressed organ.

39. The use of any one of claims 1 to 36, wherein the human recipient exhibits 25% to 50% reduced systemic inflammation post transplantation, compared to transplantation with a non-cross-dressed organ.

40. The use of any one of claims 1 to 36, wherein the human recipient exhibits 50% to 75% reduced systemic inflammation post transplantation, compared to transplantation with a non-cross-dressed organ.

41. The use of any one of claims 1 to 36, wherein the human recipient exhibits 75% to 80% reduced systemic inflammation post transplantation, compared to transplantation with a non-cross-dressed organ.

42. The use of any one of claims 1 to 36, wherein the human recipient exhibits 80% to 85% reduced systemic inflammation post transplantation, compared to transplantation with a non-cross-dressed organ.

43. The use of any one of claims 1 to 36, wherein the human recipient exhibits 85% to 90% reduced systemic inflammation post transplantation, compared to transplantation with a non-cross-dressed organ.

44. The use of any one of claims 1 to 36, wherein the human recipient exhibits at least 90% reduced systemic inflammation post transplantation, compared to transplantation with a non-cross-dressed organ.

45. The use of any one of claims 1 to 44, wherein the organ is a kidney.

46. The use of any one of claims 1 to 44, wherein the organ is a lung.

47. The use of claim 45, wherein the human recipient suffers from renal failure.

48. The use of any one of claims 1 to 47, wherein the human recipient requires less immunosuppressive therapy than the standard of care in a comparable clinical setting.

49. The use of any one of claims 1 to 47, wherein the human recipient requires 10-20% less immunosuppressive therapy than the standard of care in a comparable clinical setting.

50. The use of any one of claims 1 to 47, wherein the human recipient requires 20-30% less immunosuppressive therapy than the standard of care in a comparable clinical setting.

51. The use of any one of claims 1 to 47, wherein the human recipient requires 30-40% less immunosuppressive therapy than the standard of care in a comparable clinical setting.

52. The use of any one of claims 1 to 47, wherein the human recipient requires 40-50% less immunosuppressive therapy than the standard of care in a comparable clinical setting.

53. The use of any one of claims 1 to 47, wherein the human recipient requires 50-60% less immunosuppressive therapy than the standard of care in a comparable clinical setting.

54. The use of any one of claims 1 to 47, wherein the human recipient requires 60-70% less immunosuppressive therapy than the standard of care in a comparable clinical setting.

55. The use of any one of claims 1 to 47, wherein the human recipient requires 70-80% less immunosuppressive therapy than the standard of care in a comparable clinical setting.

56. The use of any one of claims 1 to 47, wherein the human recipient requires 80-90% less immunosuppressive therapy than the standard of care in a comparable clinical setting.

57. The use of any one of claims 1 to 47, wherein the human recipient requires at least 90% less immunosuppressive therapy than the standard of care in a comparable clinical setting.

58. The use of any one of claims 1 to 47, wherein the use results in a reduction of proteinuria.

59. The use of any one of claims 1 to 47, wherein the proteinuria is reduced to less than 3 g per 24 hours.

60. The use of any one of claims 1 to 47, wherein the proteinuria is reduced to 500 mg per 24 hours.
61. The use of any one of claims 1 to 47, wherein the proteinuria is reduced to 300 mg per 24 hours.
62. The use of any one of claims 1 to 47, wherein the proteinuria is reduced to 150 mg per 24 hours.
63. The use of any one of claims 1 to 47, wherein the proteinuria resolves within two weeks of the transplant.
64. The use of any one of claims 1 to 47, wherein the proteinuria resolves within one month of the transplant.
65. The use of any one of claims 1 to 47, wherein the proteinuria resolves within two months of the transplant.
66. The use of any one of claims 1 to 47, wherein the proteinuria resolves within four months of the transplant.
67. The use of any one of claims 1 to 66, wherein the medicament is to be further administered with transplantation of bone marrow tissue into the recipient.
68. The use of claim 67, wherein the bone marrow is taken from the same swine as the kidney.
69. The use of claim 67, wherein the bone marrow is taken from a different swine than the kidney.
70. The use of claim 67, wherein the bone marrow is cross-dressed with human CD47 by exposure to EVs comprising human CD47.
71. The use of any one of claims 1 to 70, wherein the organ does not express human SIRP α .

72. A composition comprising:
- (a) an organ from a donor swine, and
 - (b) extracellular vesicles (EVs) comprising human CD47.
73. The composition of claim 72, wherein the EVs are isolated from human cells.
74. The composition of claim 73, wherein the cells express recombinant human CD47.
75. The composition of any one of claims 72 to 74, wherein the organ is a kidney.
76. The composition of any one of claims 72 to 74, wherein the organ is a lung.
77. An *ex vivo* method of expressing human CD47 on an organ from a donor swine, wherein the method comprises:
- (a) contacting the organ from the donor swine with extracellular vesicles (EVs) comprising human CD47, and
 - (b) incubating the organ with the EVs for an amount of time sufficient to increase expression of human CD47.
78. The method of claim 77, wherein the EVs are isolated from human cells.
79. The method of claim 77 or 78, wherein incubating is for:
- (a) 1 to 12 hours;
 - (b) 12 to 16 hours;
 - (c) 16 to 24 hours; or
 - (d) more than 24 hours.
80. The method of any one of claims 77 to 79, wherein the method is achieved by *ex vivo* perfusing the organ.
81. The method of any one of claims 77 to 80, wherein the organ is a kidney or a lung.