CLAIMS

1. Use of at least one TLR2 inhibitor or a pharmaceutically acceptable salt or prodrug thereof, and at least one TLR4 inhibitor or a pharmaceutically acceptable salt or prodrug thereof in the manufacture of a medicament for treating a lung disorder, a lung disease or a lung injury; wherein the TLR2 inhibitor comprises a nucleic acid molecule targeting a TLR2 gene and the TLR4 inhibitor comprises a nucleic acid molecule targeting a TLR4 gene.

2. The use according to claim 1, wherein the lung disorder, lung disease or lung injury is selected from the group consisting of acute respiratory distress syndrome (ARDS), acute lung injury, idiopathic pulmonary fibrosis, bleomycin induced pulmonary fibrosis, mechanical ventilator induced lung injury, chronic obstructive pulmonary disease (COPD), chronic bronchitis, a disorder associated with lung transplantation and emphysema.

3. The use according to claim 2, wherein the lung disorder, lung disease or lung injury is a lung disorder associated with lung transplantation.

4. The use according to claim 3, wherein the lung disorder associated with lung transplantation is selected from the group consisting of inflammation, graft rejection, primary graft failure, ischemia-reperfusion injury, reperfusion injury, reperfusion edema, allograft dysfunction, acute graft dysfunction, pulmonary reimplantation response, bronchiolitis obliterans and primary graft dysfunction (PGD).

5. The use according to claim 4, wherein the lung disorder associated with lung transplantation is PGD.

6. The use according to any one of claims 1-5, wherein the at least one TLR2 inhibitor and the at least one TLR4 inhibitor are for co-administering to a recipient in a single formulation.

7. The use according to any one of claims 1-5, wherein the at least one TLR2 inhibitor and the at least one TLR4 inhibitor are for co-administering to a recipient in separate formulations.

8. The use according to any one of claims 6-7, wherein the at least one TLR2 inhibitor and the at least one TLR4 inhibitor are for administering to the recipient by a method selected from the group consisting of intravenous, intraarterial, intraperitoneal,

intramuscular, intraportal, subcutaneous, direct injection, intratracheal instillation, inhalation, intranasal, pulmonary and administration into the lung.

9. The use according to claim 8, wherein the at least one TLR2 inhibitor and the at least one TLR4 inhibitor are for administering to the recipient by inhalation.

10. The use according to claims 8, wherein the at least one TLR2 inhibitor and the at least one TLR4 inhibitor are for administering to the recipient by intratracheal instillation.

11. The use according to claim 1, wherein the nucleic acid molecule is selected from the group consisting of a short interfering nucleic acid (siNA), short interfering RNA (siRNA), double-stranded RNA (dsRNA), micro-RNA (miRNA) or short hairpin RNA (shRNA).

12. The use according to claim 11, wherein the TLR2 inhibitor is a double-stranded oligonucleotide comprising:

(a) a sense strand and an antisense strand;

(b) each strand is independently 17 to 40 nucleotides in length;

(c) a 17 to 40 nucleotide sequence of the antisense strand is complementary to a sequence of an mRNA encoding TLR2; and

(d) a 17 to 40 nucleotide sequence of the sense strand is complementary to the antisense strand; and

wherein the TLR4 inhibitor is a double-stranded oligonucleotide comprising:

(a) a sense strand and an antisense strand;

(b) each strand is independently 17 to 40 nucleotides in length;

(c) a 17 to 40 nucleotide sequence of the antisense strand is complementary to a sequence of an mRNA encoding TLR4; and

(d) a 17 to 40 nucleotide sequence of the sense strand is complementary to the antisense strand.

13. The use according to claim 12, wherein at least one double-stranded oligonucleotide comprises a structure (A1):

(A1) 5' (N)x – Z 3' (antisense strand)

3' Z'-(N')y –z" 5' (sense strand)

wherein each of N and N' is an unmodified ribonucleotide, a modified ribonucleotide, or an unconventional moiety;

wherein each of (N)x and (N')y is an oligonucleotide in which each consecutive N or N' is joined to the next N or N' by a covalent bond;

wherein each of Z and Z' is independently present or absent, but if present is independently 1-5 consecutive nucleotides or unconventional moieties or a combination thereof covalently attached at the 3' terminus of the strand in which it is present;

wherein z" may be present or absent, but if present is a capping moiety covalently attached at the 5' terminus of (N')y; wherein each of x and y is independently an integer between 17 and 40;

wherein the sequence of (N')y is complementary to the sequence of (N)x; and wherein (N)x comprises an antisense sequence to an mRNA selected from an mRNA encoding TLR2 and an mRNA encoding TLR4,

wherein the sequence of mRNA encoding TLR2 is set forth in SEQ ID NO:1 and wherein the sequence of mRNA encoding TLR4 is set forth in any one of SEQ ID NO:2, SEQ ID NO:3 and SEQ ID NO:4.

14. The use according to claim 13, wherein (N)x comprises an antisense oligonucleotide selected from the group consisting of oligonucleotides having SEQ ID NOs: 723-1440, 2247-3052, 7076-8312 and 8459-8604 and wherein (N')y comprises a sense strand oligonucleotide selected from the group consisting of oligonucleotides having SEQ ID NOs: 5 - 722, 1441 - 2246, 5839 – 7075 and 8313 – 8458.

15. The use according to any one of claims 13-14, wherein x = y =19.

16. The use according to claim 12, wherein, at least one double-stranded oligonucleotide comprises a structure (A2):

(A2) 5' N1-(N)x - Z 3' (antisense strand)

3' Z'-N2-(N')y–z" 5' (sense strand)

wherein each of N2, N and N' is independently an unmodified ribonucleotide, a modified ribonucleotide, or an unconventional moiety;

wherein each of (N)x and (N')y is an oligonucleotide in which each consecutive N or N' is joined to the adjacent N or N' by a covalent bond;

wherein each of x and y is independently an integer between 17 and 39;

wherein the sequence of (N')y is complementary to the sequence of (N)x and wherein (N)x is complementary to a consecutive sequence in an mRNA selected from an mRNA encoding TLR2 and an mRNA encoding TLR4;

wherein N1 is covalently bound to (N)x and is mismatched to the mRNA selected from an mRNA encoding TLR2 and an mRNA encoding TLR4;

wherein the sequence of mRNA encoding TLR2 is set forth in SEQ ID NO:1 and wherein the sequence of mRNA encoding TLR4 is set forth in any one of SEQ ID NO:2, SEQ ID NO:3 and SEQ ID NO:4;

wherein N1 is a moiety selected from the group consisting of uridine, modified uridine, ribothymidine, modified ribothymidine, deoxyribothymidine, modified deoxyribothymidine, riboadenine, deoxyriboadenine and modified deoxyriboadenine,

wherein z" may be present or absent, but if present is a capping moiety covalently attached at the 5' terminus of N2- (N')y; and

wherein each of Z and Z' is independently present or absent, but if present is independently 1-5 consecutive nucleotides or unconventional moieties or a combination thereof covalently attached at the 3' terminus of the strand in which it is present.

17. The use according to claim 16, wherein x =y=18.

18. The use according to claim 16 or 17, wherein the sequence of (N)x comprises an antisense oligonucleotide selected from the group consisting of oligonucleotides having SEQ ID NOs: 4153 – 5252, 5546 – 5838, 10319 – 12032, and 12085 – 12136 and wherein the sequence of (N')y comprises a sense oligonucleotide selected from the group consisting of oligonucleotides having SEQ ID NOs: 3053 – 4152, 5253 – 5545, 8605 – 10318, and 12033 – 12084.

19. Use of at least one TLR2 inhibitor or a pharmaceutically acceptable salt or prodrug thereof in the manufacture of a medicament for preventing or reducing the symptoms of primary graft dysfunction (PGD) in a recipient of lung transplant; wherein the TLR2 inhibitor comprises a nucleic acid molecule targeting a TLR2 gene.

20. The use according to claim 19, wherein the recipient of a lung transplant is a human that is being treated for primary graft dysfunction (PGD).

21. The use according to claim 20, wherein the medicament is for preventing or reducing the symptoms of cold ischemia-associated PGD or warm ischemia-associated PGD.

22. The use according to claim 19, wherein the symptoms are selected from the group consisting of inflammation, acute graft rejection, graft rejection, ischemia-reperfusion injury, reperfusion injury, impaired pulmonary function, bronchiolitis obliterans, impaired blood oxygenation, increased inflammatory cytokine production, intra-graft and intra-airway accumulation of granulocytes, pulmonary edema and hypoxemia.

23. The use according to any of claim 19-22, wherein the medicament is for administering to a recipient by systemic administration or local administration.

24. The use according to claim 23, wherein the medicament is for administering to the recipient by a method selected from the group consisting of intravenous, intraarterial, intraperitoneal, intramuscular, intraportal, subcutaneous, direct injection, intratracheal instillation, inhalation, intranasal, pulmonary and administration into the lung.

25. The use according to claim 24, wherein the medicament is for administering to the recipient by inhalation or intratracheal instillation.

26. The use according to claim 19, wherein the nucleic acid molecule comprises a double-stranded oligonucleotide.

27. The use according to claim 26, wherein the double-stranded oligonucleotide comprises:

(a) a sense strand and an antisense strand;

(b) each strand is independently 17 to 40 nucleotides in length;

(c) a 17 to 40 nucleotide sequence of the antisense strand is complementary to a sequence of an mRNA encoding TLR2; and

(d) a 17 to 40 nucleotide sequence of the sense strand is complementary to the antisense strand.

28. The use according to any one of claims 26-27, wherein the double-stranded oligonucleotide comprises a structure (A1):

(A1) 5' (N)x – Z 3' (antisense strand)

3' Z'-(N')y –z" 5' (sense strand)

wherein each of N and N' is an unmodified ribonucleotide, a modified ribonucleotide, or an unconventional moiety;

wherein each of (N)x and (N')y is an oligonucleotide in which each consecutive N or N' is joined to the next N or N' by a covalent bond;

wherein each of Z and Z' is independently present or absent, but if present is independently 1-5 consecutive nucleotides or unconventional moieties or a combination thereof covalently attached at the 3' terminus of the strand in which it is present;

wherein z" may be present or absent, but if present is a capping moiety covalently attached at the 5' terminus of (N')y; wherein each of x and y is independently an integer between 17 and 40;

wherein the sequence of (N')y is complementary to the sequence of (N)x; and wherein (N)x comprises an antisense sequence to an mRNA encoding TLR2 having a sequence set forth in SEQ ID NO:1.

29. The use according to claim 28, wherein (N)x comprises an antisense oligonucleotide present in SEQ ID NOs: 723-1440 and 2247-3052 and wherein (N')y comprises a sense strand oligonucleotide present in SEQ ID NOs: 5 – 722 and 1441 - 2246.

30. The use according to any one of claims 28-29, wherein x = y =19.

31. The use according to any one of claims 26-27, wherein, the double-stranded oligonucleotide comprises a structure (A2):

(A2) 5' N1-(N)x - Z 3' (antisense strand)

3' Z'-N2-(N')y–z" 5' (sense strand)

wherein each of N2, N and N' is independently an unmodified ribonucleotide, a modified ribonucleotide, or an unconventional moiety;

wherein each of (N)x and (N')y is an oligonucleotide in which each consecutive N or N' is joined to the adjacent N or N' by a covalent bond;

wherein each of x and y is independently an integer between 17 and 39;

wherein the sequence of (N')y is complementary to the sequence of (N)x and wherein (N)x is complementary to a consecutive sequence in an mRNA encoding TLR2;

wherein the sequence of mRNA encoding TLR2 is set forth in SEQ ID NO:1;

wherein N1 is covalently bound to (N)x and is mismatched to the mRNA encoding TLR2;

wherein N1 is a moiety selected from the group consisting of uridine, modified uridine, ribothymidine, modified ribothymidine, deoxyribothymidine, modified deoxyribothymidine, riboadenine, deoxyriboadenine and modified deoxyriboadenine,

wherein z" may be present or absent, but if present is a capping moiety covalently attached at the 5' terminus of N2- (N')y; and

wherein each of Z and Z' is independently present or absent, but if present is independently 1-5 consecutive nucleotides or unconventional moieties or a combination thereof covalently attached at the 3' terminus of the strand in which it is present.

32. The use according to claim 31, wherein x =y=18.

33. The use according to claim 31, wherein the sequence of (N)x is selected from anyone of SEQ ID NOs: 4153 – 5252 and 5546 – 5838 and wherein the sequence of (N')y is selected from anyone of SEQ ID NOs: 3053 – 4152 and 5253 – 5545.

CLAIMS

That which is claimed is:

1. Use of at least one TLR2 inhibitor or a pharmaceutically acceptable salt or prodrug thereof and at least one TLR4 inhibitor or a pharmaceutically acceptable salt or prodrug thereof, in the manufacture of a medicament for preventing or reducing the symptoms of primary graft dysfunction (PGD) in a recipient of a lung transplant; wherein the at least one TLR2 inhibitor or a pharmaceutically acceptable salt or prodrug thereof, and the at least one TLR4 inhibitor or a pharmaceutically acceptable salt or prodrug thereof are to be administered to the recipient..

2. The use of claim 1, wherein the recipient of the lung transplant is a human that is at risk of developing or is being treated for primary graft dysfunction (PGD).

3. The use of claim 1, for preventing or reducing the symptoms of cold ischemia-associated PGD.

4. The use of claim 1, for preventing or reducing the symptoms of warm ischemia-associated PGD.

5. The use of any of claims 1-4, wherein the symptoms are selected from the group consisting of inflammation, acute graft rejection, graft rejection, ischemia-reperfusion injury, reperfusion injury, impaired pulmonary function, bronchiolitis obliterans, impaired blood oxygenation, increased inflammatory cytokine production, intra-graft and intra-airway accumulation of granulocytes, pulmonary edema and hypoxemia.

6. The use of any of claims 1-4, wherein the administration of the at least oneTLR2 inhibitor or a pharmaceutically acceptable salt or prodrug thereof, and the at least one TLR4 inhibitor or a pharmaceutically acceptable salt or prodrug thereof results in reduced pulmonary edema in the recipient.

7. The use of any of claims 1-4, wherein the administration of the at least one TLR2 inhibitor or a pharmaceutically acceptable salt or prodrug thereof, and the at least one TLR4 inhibitor or a pharmaceutically acceptable salt or prodrug thereof results in increased blood oxygenation in the recipient.

~~8. The use of any of claims 1-4, wherein the administration of the at least one TLR2 inhibitor or a~~ pharmaceutically acceptable salt or prodrug thereof, and the least one TLR4 inhibitor or a pharmaceutically acceptable salt or prodrug thereof results in preserved blood oxygenation in the recipient.

9. The use of any of claims 1-4, wherein the administration of the at least one TLR2 inhibitor or a pharmaceutically acceptable salt or prodrug thereof, and the at least one TLR4 inhibitor or a pharmaceutically acceptable salt or prodrug thereof results in improved pulmonary function in the recipient.

10. The use of any of claims 1-4, wherein the administration of the at least one TLR2 inhibitor or a pharmaceutically acceptable salt or prodrug thereof, and the at least one TLR4 inhibitor or a pharmaceutically acceptable salt or prodrug thereof results in preserving pulmonary function in the recipient.

11. The use of any of claims 1-4, wherein the administration of the at least one TLR2 inhibitor or a pharmaceutically acceptable salt or prodrug thereof, and the at least one TLR4 inhibitor or a pharmaceutically acceptable salt or prodrug thereof results in improved pulmonary function of the transplanted lung.

12. The use of claim 1, wherein the at least one TLR2 inhibitor and the at least one TLR4 inhibitor are to be administered to the recipient of a lung transplant prior to, during or following lung transplantation.

13. The use of claim 12, wherein the at least one TLR2 inhibitor and the at least one TLR4 inhibitor are to be administered to the recipient of a lung transplant prior to lung transplantation.

14. The use of claim 12, wherein the at least one TLR2 inhibitor and the at least one TLR4 inhibitor are to be administered to the recipient of a lung transplant during lung transplantation.

~~15. The use of claim 12, wherein the at least one TLR2 inhibitor and the at least one TLR4 inhibitor~~ are to be administered to the recipient of a lung transplant following lung transplantation.

16. The use of claim 1, wherein the at least one TLR2 inhibitor and the at least one TLR4 inhibitor are to be co-administered to the recipient in the same formulation.

17. The use of claim 1, wherein the at least one TLR2 inhibitor and the at least one TLR4 inhibitor are to be co-administered to the recipient in different formulations.

18. The use of claim 1, wherein the at least one TLR2 inhibitor and the at least one TLR4 inhibitor are to be co-administered to the recipient by the same route.

19. The use of claim 1, wherein the at least one TLR2 inhibitor and the at least one TLR4 inhibitor are to be co-administered to the recipient by different routes.

20. The use of claim 1, wherein the administration to the recipient is simultaneous.

21. The use of claim 1, wherein the administration to the recipient is sequential.

22. The use of any of claims 1-21, wherein the recipient is to be administered with at least one additional treatment selected from the group consisting of surgery, steroid therapy, non-steroid therapy, antiviral therapy, antifungal therapy, antimicrobial therapy, immunosuppressant therapy, anti-infective therapy, anti-hypertensive therapy, nutritional supplements and any combination thereof.

23. The use of claim 22, wherein the additional treatment is to be administered prior to, subsequent to or concomitantly with the administration of at least one TLR2 inhibitor and at least one TLR4 inhibitor.

24. The use of claim 22 wherein the additional treatment comprises immunosuppressant therapy.

~~25. The use of claim 1, wherein the administration to the recipient comprises systemic administration~~ or local administration.

26. The use of claim 25, wherein the administration to the recipient comprises systemic administration.

27. The use of claim 25, wherein the administration to the recipient comprises local administration.

28. The use of claim 25, wherein the administration to the recipient comprises a method selected from intravenous, intraarterial, intraperitoneal, intramuscular, intraportal, subcutaneous, direct injection, intratracheal instillation, inhalation, intranasal, pulmonary and administration via pump into the lung.

29. The use of claim 28, wherein the administration to the recipient comprises inhalation.

30. The use of claim 28, wherein the administration to the recipient comprises intratracheal instillation.

31. The use of any of claims 1-30, wherein each inhibitor is independently selected from the group consisting of a small organic molecule, a protein, an antibody or fragment thereof, a peptide, a peptidomimetic and a nucleic acid molecule.

32. The use of claim 31, wherein at least one inhibitor comprises a nucleic acid molecule.

33. The use of claim 32, wherein each inhibitor comprises a nucleic acid molecule.

34. The use of claim 33, wherein a first nucleic acid molecule is a double- stranded oligonucleotide that binds a nucleotide sequence encoding a TLR2 gene and a second nucleic acid molecule is a double-stranded oligonucleotide that binds a nucleotide sequence encoding a TLR4 gene.

~~35. The use of claim 34, wherein the double-stranded oligonucleotides are linked one to the other in~~ tandem or annealed in RNAistar formation.

36. The use of claim 34, wherein the first double-stranded oligonucleotide comprises:

(a) a sense strand and an antisense strand;

(b) each strand is independently 17 to 40 nucleotides in length;

(c) a 17 to 40 nucleotide sequence of the antisense strand is complementary to a sequence of an mRNA encoding TLR2; and

(d) a 17 to 40 nucleotide sequence of the sense strand is complementary to the antisense strand; and

wherein the second double-stranded oligonucleotide comprises:

(a) a sense strand and an antisense strand;

(b) each strand is independently 17 to 40 nucleotides in length;

(c) a 17 to 40 nucleotide sequence of the antisense strand is complementary to a sequence of an mRNA encoding TLR4; and

(d) a 17 to 40 nucleotide sequence of the sense strand is complementary to the antisense strand.

37. The use of claim 36, wherein the first double-stranded oligonucleotide and the second double-stranded oligonucleotide are to be co-administered to the recipient in the same formulation.

38. The use of claim 36, wherein the first double-stranded oligonucleotide and the second double-stranded oligonucleotide are to be co-administered to the recipient in different formulations.

39. The use of claim 36, wherein the first double-stranded oligonucleotide and the second double-stranded oligonucleotide are to be co-administered to the recipient by the same route.

40. The use of claim 36, wherein the first double-stranded oligonucleotide and the second double-stranded oligonucleotide are to be co-administered to the recipient by different routes.

41. The use of claim 36, wherein the administration to the recipient is simultaneous.

42. The use of claim 36, wherein the administration to the recipient is sequential.

43. The use of claim 36, wherein the first double-stranded oligonucleotide and the second double-stranded oligonucleotide are formulated for administration to the recipient once.

44. The use of claim 36, wherein the first double-stranded oligonucleotide and the second double-stranded oligonucleotide are formulated for administration to the recipient at least once-a-day.

45. The use of claim 36, wherein the first double-stranded oligonucleotide and the second double-stranded oligonucleotide are formulated for multiple administrations to the recipient.

46. The use of claim 34, wherein at least one double-stranded oligonucleotide independently comprises a structure (Al):

(Al) 5' (N)x - Z 3' (antisense strand)

3' Z'-(N')y -z" 5' (sense strand)

wherein each of N and N' is a ribonucleotide which may be unmodified or modified, or an unconventional moiety;

wherein each of (N)x and (N')y is an oligonucleotide in which each consecutive N or N' is joined to the next N or N' by a covalent bond;

wherein each of Z and Z' is independently present or absent, but if present is independently 1-5 consecutive nucleotides or unconventional moieties or a combination thereof covalently attached at the 3 ' terminus of the strand in which it is present;

~~wherein z" may be present or absent, but if present is a capping moiety covalently attached at the~~ 5' terminus of (N')y; wherein each of x and y is independently an integer between 17 and 40; wherein the sequence of (N')y is complementary to the sequence of (N)x; and wherein (N)x comprises an antisense sequence to an mRNA selected from an mRNA encoding TLR2 and an mRNA encoding TLR4.

47. The use of claim 34 or 46, wherein the mRNA polynucleotide sequence of TLR2 is set forth in SEQ ID NO: 1 and wherein the mRNA polynucleotide sequence of TLR4 is set forth in any one of SEQ ID NO:2, SEQ ID NO:3 and SEQ ID NO:4.

48. The use of claim 46, wherein (N)x comprises an antisense oligonucleotide selected from the group consisting of oligonucleotides having SEQ ID NOs: 723-1440, 2247-3052, 7076-8312 and 8459-8604 and wherein (N')y comprises a complementary sense strand oligonucleotide selected from the group consisting of oligonucleotides having SEQ ID NOs: 5 - 722, 1441 - 2246, 5839 - 7075 and 8313 - 8458.

49. The use of claim 34 or 46, wherein administration of the at least one double-stranded oligonucleotide that binds a nucleotide sequence encoding a TLR2 gene and the at least one double-stranded oligonucleotide that binds a nucleotide sequence encoding a TLR4 gene results in down-regulation of TLR2 expression and TLR4 expression, respectively.

50. The use of any of claims 46 to 48, wherein x = y =19.

51. The use of claim 34 wherein, at least one double-stranded compound independently comprises a structure (A2):

(A2) 5' Nl-(N)x - Z 3' (antisense strand)

3' Z'-N2-(N')y-z" 5' (sense strand)

wherein each of N2, N and N' is independently an unmodified or modified ribonucleotide, or an unconventional moiety;

wherein each of (N)x and (N')y is an oligonucleotide in which each consecutive N or N' is joined to the adjacent N or N' by a covalent bond;

wherein each of x and y is independently an integer between 17 and 39;

~~wherein the sequence of (N')y is complementary to the sequence of (N)x and wherein (N)x is~~ complementary to a consecutive sequence in an mRNA selected from an mRNA encoding TLR2 and an mRNA encoding TLR4;

wherein Nl is covalently bound to (N)x and is mismatched to the mRNA selected from an mRNA encoding TLR2 and an mRNA encoding TLR4;

wherein Nl is a moiety selected from the group consisting of uridine, modified uridine, ribothymidine, modified ribothymidine, deoxyribothymidine, modified deoxyribothymidine, riboadenine, deoxyriboadenine and modified deoxyriboadenine, wherein z" may be present or absent, but if present is a capping moiety covalently attached at the 5' terminus of N2- (N')y; and

wherein each of Z and Z' is independently present or absent, but if present is independently 1-5 consecutive nucleotides or unconventional moieties or a combination thereof covalently attached at the 3' terminus of the strand in which it is present.

52. The use of claim 51, wherein x =y= 18.

53. The use of claim 51 or 52, wherein the sequence of (N)x comprises an antisense strand oligonucleotide selected from the group consisting of oligonucleotides having SEQ ID NOs: 4153 - 5252, 5546 - 5838, 10319 - 12032, and 12085 - 12136.

54. The use of claim 53, wherein the sequence of (N')y comprises a sense strand oligonucleotide selected from the group consisting of oligonucleotides having SEQ ID NOs: 3053 - 4152, 5253 - 5545, 8605 - 10318, and 12033 - 12084.

55. Use of a of at least one TLR2 inhibitor or a pharmaceutically acceptable salt or prodrug thereof, and at least one TLR4 inhibitor or a pharmaceutically acceptable salt or prodrug thereof in the manufacture of a medicament for treating a lung disorder, disease or injury in a patient in need thereof; wherein the at least one TLR2 inhibitor or a pharmaceutically acceptable salt or prodrug thereof and the at least one TLR4 inhibitor or a pharmaceutically acceptable salt or prodrug thereof are to be administered to the patient.

56. The use of claim 55, wherein the lung disorder, disease or injury is selected from acute respiratory distress syndrome (ARDS), acute lung injury, pulmonary fibrosis (idiopathic), bleomycin induced pulmonary fibrosis, mechanical ventilator induced

~~lung injury, chronic obstructive pulmonary disease (COPD), chronic bronchitis, a disorder~~ associated with lung transplantation and emphysema.

57. The use of claim 56, wherein the lung disorder, disease or injury is a disorder associated with lung transplantation.

58. The use of claim 57, wherein the lung disorder associated with lung transplantation is selected from the group consisting of inflammation, graft rejection, primary graft failure, ischemia-reperfusion injury, reperfusion injury, reperfusion edema, allograft dysfunction, acute graft dysfunction, pulmonary reimplantation response, bronchiolitis obliterans and primary graft dysfunction (PGD).

59. The use of claim 58, wherein the lung disorder associated with lung transplantation is PGD.

60. The use of any of claims 55-59, wherein the at least one TLR2 inhibitor and the at least one TLR4 inhibitor are to be co-administered to the recipient in the same formulation.

61. The use of any of claims 55-59, wherein the at least one TLR2 inhibitor and the at least one TLR4 inhibitor are to be co-administered to the recipient in different formulations.

62. The use of any of claims 55-59, wherein the at least one TLR2 inhibitor and the at least one TLR4 inhibitor are to be co-administered to the recipient by the same route.

63. The use of any of claims 55-59, wherein the at least one TLR2 inhibitor and the at least one TLR4 inhibitor are to be co-administered to the recipient by different routes.

64. The use of any of claims 55-59, wherein the administration to the recipient is simultaneous.

65. The use of any of claims 55-59, wherein the administration to the recipient is sequential.

~~66. The use of any of claims 55-65, wherein the patient is to be administered with at least one~~ additional treatment selected from the group consisting of surgery, steroid therapy, non-steroid therapy, antiviral therapy, antifungal therapy, antimicrobial therapy, immunosuppressant therapy, anti-infective therapy, anti-hypertensive therapy, nutritional supplements and any combination thereof.

67. The use of claim 66, wherein the additional treatment is to be administered prior to, subsequent to or concomitantly with the administration of at least one TLR2 inhibitor and at least one TLR4 inhibitor.

68. The use of claim 67, wherein the additional treatment comprises immunosuppressant therapy.

69. The use of any of claims 55-65, wherein the administration to the patient comprises systemic administration or local administration.

70. The use of claim 69, wherein the administration to the patient comprises systemic administration.

71. The use of claim 69, wherein the administration to the patient comprises local administration.

72. The use of claim 69,wherein the administration to the patient comprises a method selected from intravenous, intraarterial, intraperitoneal, intramuscular, intraportal, subcutaneous, direct injection, intratracheal instillation, inhalation, intranasal, pulmonary and administration via pump into the lung.

73. The use of claim72, wherein the administration to the patient comprises inhalation.

74. The use of claim72, wherein the administration to the patient comprises intratracheal instillation.

75. ~~The use of claim 55, wherein each inhibitor is independently selected from the group consisting~~ of a small organic molecule, a protein, an antibody or fragment thereof, a peptide, a peptidomimetic and a nucleic acid molecule.

76. The use of claim 75, wherein at least one inhibitor comprises a nucleic acid molecule.

77. The use of claim 76, wherein each inhibitor comprises a nucleic acid molecule.

78. The use of claim 77, wherein a first nucleic acid molecule is a double- stranded oligonucleotide that binds a nucleotide sequence encoding a TLR2 gene and a second nucleic acid molecule is a double-stranded oligonucleotide that binds a nucleotide sequence encoding a TLR4 gene.

79. The use of claim 77, wherein the double-stranded oligonucleotides are linked one to the other in tandem or annealed in RNAistar formation.

80. The use of claim 78, wherein the first double-stranded oligonucleotide comprises:

(a) a sense strand and an antisense strand;

(b) each strand is independently 17 to 40 nucleotides in length;

(c) a 17 to 40 nucleotide sequence of the antisense strand is complementary to a sequence of an mRNA encoding TLR2; and

(d) a 17 to 40 nucleotide sequence of the sense strand is complementary to the antisense strand; and

wherein the second double-stranded oligonucleotide comprises:

(a) a sense strand and an antisense strand;

(b) each strand is independently 17 to 40 nucleotides in length;

(c) a 17 to 40 nucleotide sequence of the antisense strand is complementary to a sequence of an mRNA encoding TLR4; and

(d) a 17 to 40 nucleotide sequence of the sense strand is complementary to the antisense strand.

~~81. The use of claim 80, wherein the first double-stranded oligonucleotide and the second double-~~ stranded oligonucleotide are to be co-administered to the patient in the same formulation.

82. The use of claim 80, wherein the first double-stranded oligonucleotide and the second double-stranded oligonucleotide are to be co-administered to the patient in different formulations.

83. The use of claim 80, wherein the first double-stranded oligonucleotide and the second double-stranded oligonucleotide are to be co-administered to the patient by the same route.

84. The use of claim 80, wherein the first double-stranded oligonucleotide and the second double-stranded oligonucleotide are to be co -administered to the patient by different routes.

85. The use of claim 80, wherein the administration to the patient is simultaneous.

86. The use of claim 80, wherein the administration to the patient is sequential.

87. The use of claim 80, wherein the first double-stranded oligonucleotide and the second double-stranded oligonucleotide are formulated for administration to the patient once.

88. The use of claim 80, wherein the first double-stranded oligonucleotide and the second double-stranded oligonucleotide are formulated for administration to the patient at least once-a-day.

89. The use of claim 80, wherein the first double-stranded oligonucleotide and the second double-stranded oligonucleotide are formulated for multiple administrations to the patient.

~~90. The use of claim 78, wherein at least one double-stranded oligonucleotide comprises a structure~~ (Al):

(Al)	5'	(N)x - Z	3'	(antisense strand)
	3'	Z'-(N')y -z"	5'	(sense strand)

wherein each of N and N' is a ribonucleotide which may be unmodified or modified, or an unconventional moiety;

wherein each of (N)x and (N')y is an oligonucleotide in which each consecutive N or N' is joined to the next N or N' by a covalent bond;

wherein each of Z and Z' is independently present or absent, but if present is independently 1-5 consecutive nucleotides or unconventional moieties or a combination thereof covalently attached at the 3 ' terminus of the strand in which it is present;

wherein z" may be present or absent, but if present is a capping moiety covalently attached at the 5' terminus of (N')y; wherein each of x and y is independently an integer between 17 and 40; wherein the sequence of (N')y is complementary to the sequence of (N)x; and wherein (N)x comprises an antisense sequence to an mRNA selected from an mRNA encoding TLR2 and an mRNA encoding TLR4.

91. The use of claim 78 or 90, wherein the mRNA polynucleotide sequence of TLR2 is set forth in SEQ ID NO: 1 and wherein the mRNA polynucleotide sequence of TLR4 is set forth in any one of SEQ ID NO:2, SEQ ID NO:3 and SEQ ID NO:4.

92. The use of claim 90, wherein (N)x comprises an antisense oligonucleotide selected from the group consisting of oligonucleotides having SEQ ID NOs: 723-1440, 2247-3052, 7076-8312 and 8459-8604 and wherein (N')y comprises a sense strand oligonucleotide selected from the group consisting of oligonucleotides having SEQ ID NOs: 5 - 722, 1441 - 2246, 5839 - 7075 and 8313 - 8458.

93. The use of any of claims 90 to 92, wherein x = y =19.

94. The use of claim 78 wherein, at least one double-stranded compound comprises a structure (A2):

(A2)	5'	Nl-(N)x - Z	3'	(antisense strand)
	3'	Z'-N2-(')y-z"	5 '	(sense strand)

wherein each of N2, N and N' is independently an unmodified or modified ribonucleotide, or an unconventional moiety;

wherein each of (N)x and (N')y is an oligonucleotide in which each consecutive N or N' is joined to the adjacent N or N' by a covalent bond;

wherein each of x and y is independently an integer between 17 and 39;

wherein the sequence of (N')y is complementary to the sequence of (N)x and wherein (N)x is complementary to a consecutive sequence in an mR A selected from an mR A encoding TLR2 and an mRNA encoding TLR4;

wherein Nl is covalently bound to (N)x and is mismatched to the mRNA selected from an mRNA encoding TLR2 and an mRNA encoding TLR4;

wherein Nl is a moiety selected from the group consisting of uridine, modified uridine, ribothymidine, modified ribothymidine, deoxyribothymidine, modified deoxyribothymidine, riboadenine, deoxyriboadenine and modified deoxyriboadenine, wherein z" may be present or absent, but if present is a capping moiety covalently attached at the 5' terminus of N2- (N')y; and

wherein each of Z and Z' is independently present or absent, but if present is independently 1-5 consecutive nucleotides or unconventional moieties or a combination thereof covalently attached at the 3 ' terminus of the strand in which it is present.

95. The use of claim 94, wherein x =y=l 8.

96. The use of claim 94 or 95, wherein the sequence of (N)x comprises an antisense oligonucleotide selected from the group consisting of oligonucleotides having SEQ ID NOs: 4153 - 5252, 5546 - 5838, 10319 - 12032, and 12085 - 12136 and wherein the sequence of (N')y comprises a sense oligonucleotide selected from the group consisting of oligonucleotides having SEQ ID NOs: 3053 - 4152, 5253 - 5545, 8605 - 10318, and 12033 - 12084.

97. A composition comprising at least one TLR2 inhibitor or a pharmaceutically acceptable salt or prodrug thereof and at least one TLR4 inhibitor or a pharmaceutically acceptable salt or prodrug thereof; and a pharmaceutically acceptable carrier.

98. The composition of claim 97, wherein each inhibitor is independently selected from the group consisting of a small organic molecule; a protein, an antibody or fragments thereof, a peptide, a peptidomimetic and a nucleic acid molecule.

~~99. The composition of claim 98, wherein each inhibitor is independently selected from the group~~ consisting of a small organic molecule; a protein; an antibody or fragment thereof; and a nucleic acid molecule.

100. The composition of claim 99, wherein each inhibitor comprises a nucleic acid molecule.

101. The composition of claim 100, wherein a first nucleic acid molecule is a double-stranded oligonucleotide that binds a nucleotide sequence encoding a TLR2 gene and a second nucleic acid molecule is a double-stranded oligonucleotide that binds a nucleotide sequence encoding a TLR4 gene.

102. The composition of claim 101, wherein the nucleic acid molecules are linked in tandem or annealed in RNAistar formation.

103. The composition of claim 101, wherein a first double-stranded oligonucleotide comprises:

(a) a sense strand and an antisense strand;

(b) each strand is independently 17 to 40 nucleotides in length;

(c) a 17 to 40 nucleotide sequence of the antisense strand is complementary to a sequence of an mRNA encoding TLR2; and

(d) a 17 to 40 nucleotide sequence of the sense strand is complementary to the antisense strand; and

wherein a second double-stranded oligonucleotide comprises:

(a) a sense strand and an antisense strand;

(b) each strand is independently 17 to 40 nucleotides in length;

(c) a 17 to 40 nucleotide sequence of the antisense strand is complementary to a sequence of an mRNA encoding TLR4; and

(d) a 17 to 40 nucleotide sequence of the sense strand is complementary to the antisense strand.

104. The composition of claim 103, wherein the amount of each double-stranded oligonucleotide in the composition independently ranges from about 0.05 mg to about 10.0 mg.

~~105. The composition of claim 101, wherein at least one double-stranded oligonucleotide~~ independently comprises a structure (Al):

(Al) 5' (N)x - Z 3' (antisense strand)

3' Z'-(N')y -z" 5' (sense strand)

wherein each of N and N' is a ribonucleotide which may be unmodified or modified, or an unconventional moiety;

wherein each of (N)x and (N')y is an oligonucleotide in which each consecutive N or N' is joined to the next N or N' by a covalent bond;

wherein each of Z and Z' is independently present or absent, but if present is independently 1-5 consecutive nucleotides or unconventional moieties or a combination thereof covalently attached at the 3 ' terminus of the strand in which it is present.

wherein z" may be present or absent, but if present is a capping moiety covalently attached at the 5' terminus of (N')y;

wherein each of x and y is independently an integer between 17 and 40;

wherein the sequence of (N')y is complementary to the sequence of (N)x; and wherein (N)x comprises an antisense sequence to an mRNA selected from an mRNA encoding TLR2 and an mRNA encoding TLR4.

106. The composition of claim 101, wherein at least one double-stranded oligonucleotide compound independently comprises a structure (A2):

(A2) 5' Nl-(N)x - Z 3' (antisense strand)

3' Z'-N2-(N')y-z" 5' (sense strand)

wherein each of N2, N and N' is independently an unmodified or modified ribonucleotide, or an unconventional moiety;

wherein each of (N)x and (N')y is an oligonucleotide in which each consecutive N or N' is joined to the adjacent N or N' by a covalent bond;

wherein each of x and y is independently an integer between 17 and 39;

wherein the sequence of (N')y is complementary to the sequence of (N)x and (N)x is complementary to a consecutive sequence in an mRNA selected from an mRNA encoding TLR2 and an mRNA encoding TLR4;

wherein Nl is covalently bound to (N)x and is mismatched to an mRNA selected from an mRNA encoding TLR2 and an mRNA encoding TLR4;

wherein N1 is a moiety selected from the group consisting of uridine, modified uridine, ribothymidine, modified ribothymidine, deoxyribothymidine, modified deoxyribothymidine, riboadenine, deoxyriboadenine and modified deoxyriboadenine, wherein z" may be present or absent, but if present is a capping moiety covalently attached at the 5' terminus of N2- (N')y; and wherein each of Z and Z' is independently present or absent, but if present is independently 1-5 consecutive nucleotides or unconventional moieties or a combination thereof covalently attached at the 3 ' terminus of the strand in which it is present.

107. The composition of any of claims 102-106, wherein the double-stranded oligonucleotides are formulated for administering once, at least once-a-day or for multiple administrations.

108. A kit comprising at least two therapeutic agents, wherein at least one agent comprises a TLR2 inhibitor and a second agent comprises a TLR4 inhibitor; optionally with instructions for use.

109. The kit of claim 108, wherein each therapeutic agent is independently selected from the group consisting of a small organic molecule, a protein, an antibody or fragment thereof, a peptide, a peptidomimetic and nucleic acid molecule.

110. The kit of claim 109, wherein at least one therapeutic agent comprises a nucleic acid molecule.

111. The kit of claim 110, wherein each therapeutic agent comprises a nucleic acid molecule.

112. The kit of claim 111, wherein a first nucleic acid molecule is a double- stranded oligonucleotide that binds a nucleotide sequence encoding a TLR2 gene and a second nucleic acid molecule is a double-stranded oligonucleotide that binds a nucleotide sequence encoding a TLR4 gene.

113. The kit of claim 112, wherein the double-stranded oligonucleotides are linked one to the other in tandem or annealed in RNAistar formation.

~~114. The kit of claim 113, wherein the first double-stranded oligonucleotide comprises:~~

(a) a sense strand and an antisense strand;

(b) each strand is independently 17 to 40 nucleotides in length;

(c) a 17 to 40 nucleotide sequence of the antisense strand is complementary to a sequence of an mRNA encoding TLR24; and

(d) a 17 to 40 nucleotide sequence of the sense strand is complementary to the antisense strand; and

wherein the second double-stranded oligonucleotide comprises:

(a) a sense strand and an antisense strand;

(b) each strand is independently 17 to 40 nucleotides in length;

(c) a 17 to 40 nucleotide sequence of the antisense strand is complementary to a sequence of an mRNA encoding TLR4; and

(d) a 17 to 40 nucleotide sequence of the sense strand is complementary to the antisense strand.

115. The kit of claim 114, wherein the first double-stranded oligonucleotide and the second double-stranded oligonucleotide are formulated for co-administration to a recipient in the same formulation.

116. The kit of claim 114, wherein the first double-stranded oligonucleotide and the second double-stranded oligonucleotide are formulated for co-administration to the recipient in different formulations.

117. The kit of claim 114, wherein the first double-stranded oligonucleotide and the second double-stranded oligonucleotide are formulated for co-administration to the recipient by the same route.

118. The kit of claim 114, wherein the first double-stranded oligonucleotide and the second double-stranded oligonucleotide are formulated for administration to the recipient by different routes.

~~119. The kit of claim 114, wherein the first double-stranded oligonucleotide and the second~~ double-stranded oligonucleotide are formulated for simultaneous administration to the recipient.

120. The kit of claim 114, wherein the first double-stranded oligonucleotide and the second double-stranded oligonucleotide are formulated for sequential administration to the recipient.

121. The kit of claim 114, wherein the first double-stranded oligonucleotide and the second double-stranded oligonucleotide are formulated for administering to the patient once, at least once-a-day or for multiple administrations to the recipient.

122. The kit of claim 114, wherein at least one double-stranded oligonucleotide independently comprises a structure (Al):

(Al) 5' (N)x - Z 3' (antisense strand)

3' Z'-(')y -z" 5' (sense strand)

wherein each of N and N' is a ribonucleotide which may be unmodified or modified, or an unconventional moiety;

wherein each of (N)x and (N')y is an oligonucleotide in which each consecutive N or N' is joined to the next N or N' by a covalent bond;

wherein each of Z and Z' is independently present or absent, but if present is independently 1-5 consecutive nucleotides or unconventional moieties or a combination thereof covalently attached at the 3 ' terminus of the strand in which it is present.

wherein z" may be present or absent, but if present is a capping moiety covalently attached at the 5' terminus of (N')y;

wherein each of x and y is independently an integer between 17 and 40;

wherein the sequence of (N')y is complementary to the sequence of (N)x; and wherein (N)x comprises an antisense sequence to an mRNA selected from an mRNA encoding TLR2 and an mRNA encoding TLR4.

123. The kit of claim 114, wherein at least one double-stranded oligonucleotide independently comprises a structure (A2):

(A2) 5' Nl-(N)x - Z 3' (antisense strand)

3' Z'-N2-(N')y-z" 5' (sense strand)

wherein each of N2, N and N' is independently an unmodified or modified ribonucleotide, or an unconventional moiety;

wherein each of (N)x and (N')y is an oligonucleotide in which each consecutive N or N' is joined to the adjacent N or N' by a covalent bond;

wherein each of x and y is independently an integer between 17 and 39;

wherein the sequence of (N')y is complementary to the sequence of (N)x and (N)x is complementary to a consecutive sequence in an mR A selected from an mRNA encoding TLR2 and an mRNA encoding TLR4;

wherein Nl is covalently bound to (N)x and is mismatched to an mRNA selected from an mRNA encoding TLR2 and an mRNA encoding TLR4;

wherein Nl is a moiety selected from the group consisting of uridine, modified uridine, ribothymidine, modified ribothymidine, deoxyribothymidine, modified deoxyribothymidine, riboadenine, deoxyriboadenine and modified deoxyriboadenine,

wherein z" may be present or absent, but if present is a capping moiety covalently attached at the 5' terminus of N2- (N')y; and

wherein each of Z and Z' is independently present or absent, but if present is independently 1-5 consecutive nucleotides or unconventional moieties or a combination thereof covalently attached at the 3 ' terminus of the strand in which it is present.

124. A package comprising A) at least two separate dosage units selected from (i) at least one dosage unit comprising a TLR2 inhibitor and (ii) at least one dosage unit comprising a TLR4 inhibitor; and optionally B) a package insert comprising instructions for use of the dosage units.

125. The package of claim 124, wherein the TLR2 inhibitor is a double-stranded oligonucleotide that binds a nucleotide sequence encoding a TLR2 gene and the TLR4 inhibitor is a double-stranded oligonucleotide that binds a nucleotide sequence encoding a TLR4 gene.

126. The package of claim 125, wherein the TLR2 inhibitor is a double-stranded oligonucleotide comprising:

(a) a sense strand and an antisense strand;

(b) each strand is independently 17 to 40 nucleotides in length;

(c) a 17 to 40 nucleotide sequence of the antisense strand is complementary to a sequence of an mRNA encoding TLR2; and

(d) a 17 to 40 nucleotide sequence of the sense strand is complementary to the antisense strand and;

wherein the TLR4 inhibitor is a double-stranded oligonucleotide comprising:

(a) a sense strand and an antisense strand;

(b) each strand is independently 17 to 40 nucleotides in length;

(c) a 17 to 40 nucleotide sequence of the antisense strand is complementary to a sequence of an mRNA encoding TLR4; and

(d) a 17 to 40 nucleotide sequence of the sense strand is complementary to the antisense strand.

127. The package of claim 124, wherein the dosage units are to be co-administered to a patient by the same route.

128. The package of claim 124, wherein the dosage units are to be co-administered to a patient by different routes.

129. The package of claim 124, wherein the dosage units are to be administered to a patient simultaneously or sequentially.

130. The package of claim 132, wherein dosage units are for administration to a patient at least once-a-day.

131. The package of claim 124, wherein the dosage units are for multiple administrations to a patient.

132. The package of claim 124, wherein at least one double-stranded oligonucleotide independently comprises a structure (Al):

(Al) 5' (N)x - Z 3' (antisense strand)

3' Z'-(')y -z" 5' (sense strand)

wherein each of N and N' is a ribonucleotide which may be unmodified or modified, or an unconventional moiety;

wherein each of (N)x and (N')y is an oligonucleotide in which each consecutive N or N' is joined to the next N or N' by a covalent bond;

wherein each of Z and Z' is independently present or absent, but if present is independently 1-5 consecutive nucleotides or unconventional moieties or a combination thereof covalently attached at the 3 ' terminus of the strand in which it is present.

wherein z" may be present or absent, but if present is a capping moiety covalently attached at the 5' terminus of (N')y;

wherein each of x and y is independently an integer between 17 and 40;

wherein the sequence of (N')y is complementary to the sequence of (N)x; and wherein (N)x comprises an antisense sequence to an mRNA selected from an mRNA encoding TLR2 and an mRNA encoding TLR4.

133. The package of claim 124, wherein at least one double-stranded oligonucleotide independently comprises a a structure (A2):

(A2) 5' Nl-(N)x - Z 3' (antisense strand)

3' Z'-N2-(N')y-z" 5' (sense strand)

wherein each of N2, N and N' is independently an unmodified or modified ribonucleotide, or an unconventional moiety;

wherein each of (N)x and (N')y is an oligonucleotide in which each consecutive N or N' is joined to the adjacent N or N' by a covalent bond;

wherein each of x and y is independently an integer between 17 and 39;

wherein the sequence of (N')y is complementary to the sequence of (N)x and (N)x is complementary to a consecutive sequence in an mRNA selected from an mRNA encoding TLR2 and an mRNA encoding TLR4;

wherein Nl is covalently bound to (N)x and is mismatched to an mRNA selected from an mRNA encoding TLR2 and an mRNA encoding TLR4;

wherein Nl is a moiety selected from the group consisting of uridine, modified uridine, ribothymidine, modified ribothymidine, deoxyribothymidine, modified deoxyribothymidine, riboadenine, deoxyriboadenine and modified deoxyriboadenine,

wherein z" may be present or absent, but if present is a capping moiety covalently attached at the 5' terminus of N2- (N')y; and

wherein each of Z and Z' is independently present or absent, but if present is independently 1-5 consecutive nucleotides or unconventional moieties or a combination thereof covalently attached at the 3 ' terminus of the strand in which it is present.

~~134. The kit or package of any one of claims to 108-124, wherein the instructions or package~~ insert indicates that the therapeutic agents or dosage units are suitable for use in treating a patient suffering from a lung disease, injury or disorder selected from the group consisting of acute respiratory distress syndrome (ARDS), acute lung injury, pulmonary fibrosis (idiopathic), bleomycin induced pulmonary fibrosis, mechanical ventilation induced lung injury, chronic obstructive pulmonary disease (COPD), chronic bronchitis, a disorder associated with lung transplantation and emphysema.

135. The kit or package of claim 134, wherein the instructions or package insert indicate that the therapeutic agents or dosage units are suitable for use in treating a patient suffering from a disorder associated with lung transplantation.

136. The kit or package of claim 135, wherein lung disorder associated with lung transplantation is selected from the group consisting of inflammation, graft rejection, primary graft failure, ischemia-reperfusion injury, reperfusion injury, reperfusion edema, allograft dysfunction, acute graft dysfunction, pulmonary reimplantation response, bronchiolitis obliterans and primary graft dysfunction (PGD).

137. Use of at least one TLR2 inhibitor or a pharmaceutically acceptable salt or prodrug thereof in the manufacture of a medicament for preventing or reducing the symptoms of primary graft dysfunction (PGD) in a recipient of a lung transplant; whereinthe recipient is to be administered a therapeutically-effective amount of at least one TLR2 inhibitor or a pharmaceutically acceptable salt or prodrug thereof.

138. The use of claim 137, wherein the recipient of a lung transplant is a human that is being treated for primary graft dysfunction (PGD).

139. The use of claim 138, for preventing or reducing the symptoms of cold ischemia-associated PGD or warm ischemia-associated PGD.

140. The use of any of claims 137-139, wherein the symptoms are selected from the group consisting of inflammation, acute graft rejection, graft rejection, ischemia- reperfusion injury, reperfusion injury, impaired pulmonary function, bronchiolitis obliterans,

~~impaired blood oxygenation, increased inflammatory cytokine production, intra-graft and intra-~~ airway accumulation of granulocytes, pulmonary edema and hypoxemia.

141. The use of claim 137-139, wherein the administration of a therapeutically-effective amount of at least one TLR2 inhibitor or a pharmaceutically acceptable salt or prodrug thereof, results in one of reduced pulmonary edema in the recipient; increased blood oxygenation in the recipient, preserved blood oxygenation in the recipient, improved pulmonary function in the recipient, preserving pulmonary function in the recipient, improved pulmonary function of the transplanted lung.

142. The use of claim 141, wherein the at least one TLR2 inhibitor is to be administered to the recipient of a lung transplant prior to, during or following lung transplantation.

143. The use of any of claims 137-142, wherein the recipient is to be further administered with at least one additional treatment selected from the group consisting of surgery, steroid therapy, nonsteroid therapy, antiviral therapy, antifungal therapy, antimicrobial therapy, immunosuppressant therapy, anti-infective therapy, anti-hypertensive therapy, nutritional supplements and any combination thereof.

144. The use of claim 143, wherein the additional treatment is to be administered prior to, subsequent to or concomitantly with the administration of at least one TLR2 inhibitor.

145. The use of claim 143, wherein the additional treatment comprises immunosuppressant therapy.

146. The use of claim 143, wherein the administration to the recipient comprises systemic administration or local administration.

147. The use of claim 146, wherein the administration to the recipient comprises a method selected from intravenous, intraarterial, intraperitoneal, intramuscular, intraportal, subcutaneous, direct injection, intratracheal instillation, inhalation, intranasal, pulmonary and administration via pump into the lung.

148. The use of claim 147, wherein the administration to the recipient comprises inhalation or intratracheal instillation.

149. The use of claim 137, wherein the inhibitor comprises a nucleic acid molecule.

150. The use of claim 149, wherein the double-stranded oligonucleotide comprises:

(a) a sense strand and an antisense strand;

(b) each strand is independently 17 to 40 nucleotides in length;

(c) a 17 to 40 nucleotide sequence of the antisense strand is complementary to a sequence of an mRNA encoding TLR2; and

(d) a 17 to 40 nucleotide sequence of the sense strand is complementary to the antisense strand.

151. The use of claim 150, wherein the double-stranded oligonucleotide is formulated for administration to the patient once, at least once-a-day or for multiple administrations to the recipient.

152. The use of claim 151, wherein the double-stranded oligonucleotide comprises a structure (Al):

(Al) 5' (N)x - Z 3' (antisense strand)

3' Z'-(N')y -z" 5' (sense strand)

wherein each of N and N' is a ribonucleotide which may be unmodified or modified, or an unconventional moiety;

wherein each of (N)x and (N')y is an oligonucleotide in which each consecutive N or N' is joined to the next N or N' by a covalent bond;

wherein each of Z and Z' is independently present or absent, but if present is independently 1-5 consecutive nucleotides or unconventional moieties or a combination thereof covalently attached at the 3 ' terminus of the strand in which it is present.

wherein z" may be present or absent, but if present is a capping moiety covalently attached at the 5' terminus of (N')y; wherein each of x and y is independently an integer between 17 and 40;

wherein the sequence of (N')y is complementary to the sequence of (N)x; and wherein (N)x comprises an antisense sequence to an mRNA encoding TLR2 having a sequence forth in SEQ ID NO: 1 .

153. The use of claim 152, wherein (N)x comprises an antisense oligonucleotide present in SEQ ID NOs: 723-1440 and 2247-3052 and wherein (N')y comprises a sense strand oligonucleotide present in SEQ ID NOs: 5 - 722 and 1441 - 2246.

154. The use of any one of claim 152-153, wherein x = y =19.

155. The use of claim 151 wherein, the double-stranded compound comprises a structure (A2):

(A2) 5' Nl-(N)x - Z 3' (antisense strand)

3' Z'-N2-(N')y-z" 5' (sense strand)

wherein each of N2, N and N' is independently an unmodified or modified ribonucleotide, or an unconventional moiety;

wherein each of (N)x and (N')y is an oligonucleotide in which each consecutive N or N' is joined to the adjacent N or N' by a covalent bond;

wherein each of x and y is independently an integer between 17 and 39;

wherein the sequence of (N')y is complementary to the sequence of (N)x and wherein (N)x is complementary to a consecutive sequence in an mRNA encoding TLR2; wherein Nl is covalently bound to (N)x and is mismatched to the mRNA encoding TLR2;

wherein Nl is a moiety selected from the group consisting of uridine, modified uridine, ribothymidine, modified ribothymidine, deoxyribothymidine, modified deoxyribothymidine, riboadenine, deoxyriboadenine and modified deoxyriboadenine, wherein z" may be present or absent, but if present is a capping moiety covalently attached at the 5' terminus of N2- (N')y; and wherein each of Z and Z' is independently present or absent, but if present is independently 1-5 consecutive nucleotides or unconventional moieties or a combination thereof covalently attached at the 3' terminus of the strand in which it is present.

156. The use of claim 155, wherein x=y=18.

157. The use of claim 155, wherein the sequence of (N)x is selected from any one of SEQ ID NOs: 4153 - 5252 and 5546 - 5838 and wherein the sequence of (N')y is selected from any one of SEQ ID NOs: 3053 - 4152 and 5253 - 5545.

158. The use of claim 155, wherein administration of the at least one double- stranded oligonucleotide that binds a nucleotide sequence encoding a TLR2 gene results in down-regulation of TLR2 expression.

159. A kit or package comprising at least one dosage unit comprising a TLR2 inhibitor; optionally with instructions for use, wherein the instructions indicate that the dosage unit is suitable for use in treating a patient suffering from a lung disease, injury or disorder selected from the group consisting of respiratory distress syndrome (ARDS), acute lung injury, pulmonary fibrosis (idiopathic), bleomycin induced pulmonary fibrosis, mechanical ventilator induced lung injury, chronic obstructive pulmonary disease (COPD), chronic bronchitis, a disorder associated with lung transplantation and emphysema.

160. The kit or package of claim 159, wherein the TLR2 inhibitor comprises a nucleic acid molecule.

161. The kit or package of claim 160, wherein the nucleic acid molecule is a double-stranded oligonucleotide that binds a nucleotide sequence encoding a TLR2 gene.

162. The kit or package of claim 161, wherein the double-stranded oligonucleotide comprises:

(a) a sense strand and an antisense strand;

(b) each strand is independently 17 to 40 nucleotides in length;

(c) a 17 to 40 nucleotide sequence of the antisense strand is complementary to a sequence of an mRNA encoding TLR2; and

(d) a 17 to 40 nucleotide sequence of the sense strand is complementary to the antisense strand.

163. The kit or package of claim 162, wherein the double-stranded oligonucleotide is formulated for administration to the patient once, at least once-a-day or for multiple administrations to the patient.

~~164. The kit or package of claim 162, wherein the double-stranded oligonucleotide comprises~~ a structure (A1) or (A2), as disclosed in the specification.

165. A composition of any one of claims 97-107 for use in therapy.

166. A composition of claim 165 wherein the therapy comprises treating or preventing or reducing the symptoms of primary graft dysfunction (PGD) in a recipient of a lung transplant, for preventing or reducing the symptoms of cold ischemia-associated PGD, for preventing or reducing the symptoms of warm ischemia-associated PGD.

167. A composition of claim 166, wherein the symptoms are selected from the group consisting of inflammation, acute graft rejection, graft rejection, ischemia-reperfusion injury, reperfusion injury, impaired pulmonary function, bronchiolitis obliterans, impaired blood oxygenation, increased inflammatory cytokine production, intra-graft and intra-airway accumulation of granulocytes, pulmonary edema and hypoxemia.

168. Use of a composition of any one of claims 97-107 for the preparation of a medicament for treating or preventing a lung disease, disorder or injury selected from acute respiratory distress syndrome (ARDS), acute lung injury, pulmonary fibrosis (idiopathic), bleomycin induced pulmonary fibrosis, mechanical ventilator induced lung injury, chronic obstructive pulmonary disease (COPD), chronic bronchitis, and emphysema.

169. Use of a composition of any one of claims 97-107 in the manufacture of a medicament (i) for treating or preventing or reducing the symptoms of primary graft dysfunction (PGD) in a recipient of a lung transplant; (ii) for preventing or reducing the symptoms of cold ischemia-associated PGD; or (iii) for preventing or reducing the symptoms of warm ischemia-associated PGD.

170. The use of claim 169, wherein the symptoms are selected from the group consisting of inflammation, acute graft rejection, graft rejection, ischemia-reperfusion injury, reperfusion injury, impaired pulmonary function, bronchiolitis obliterans, impaired blood oxygenation, increased inflammatory cytokine production, intra-graft and intra-airway accumulation of granulocytes, pulmonary edema and hypoxemia.