CLAIMS

1. An antagonist of Toll Like Receptor 3 (TLR3) that inhibits cellular production of Regulated on Activation, Normal T-cell Expressed and Secreted (RANTES) cytokine.

2. The antagonist of claim 1 wherein cellular production of a cytokine selected from the group consisting of interleukin-6 (IL-6), interleukin-8 (IL-8) and macrophage inflammatory protein-1 alpha (MIP1-alpha) is also inhibited.

3. The antagonist of claim 1 or 2 wherein the antagonist is an antibody.

4. An isolated antibody reactive with TLR3 having the antigen binding ability of a monoclonal antibody comprising the amino acid sequences of the heavy chain complementarity determining regions (CDRs) as shown in SEQ ID NOs: 9, 11 and 13 and the amino acid sequences of the light chain CDRs as shown in SEQ ID NOs: 19, 21 and 23.

5. The isolated antibody of claim 4 comprising the amino acid sequences of the heavy chain CDRs as shown in SEQ ID NOs: 9, 11 and 13 and the amino acid sequences of the light chain CDRs as shown in SEQ ID NOs: 19, 21 and 23.

6. The isolated antibody of claim 4 comprising a heavy chain variable region (V_H) having the amino acid sequence shown in SEQ ID NO: 6 and a light chain variable region (V_L) having the amino acid sequence shown in SEQ ID NO: 16.

7. The isolated antibody of claim 4 comprising a V_H having the amino acid sequence shown in SEQ ID NO: 25, 27, 29 or 31 and a V_L amino acid sequence as shown in SEQ ID NO: 33, 35, 37 or 39.

8. The isolated antibody of claim 7 wherein the V_H has the amino acid sequence shown in SEQ ID NO: 25 and the V_L has the amino acid sequence shown in SEQ ID NO: 33.

9. An isolated antibody having a V_H CDR1 amino acid sequence as shown in Formula (I):

Thr Thr Tyr Trp Xaa_1 His

(I)

wherein Xaa_1 is Ile or Met (SEQ ID NO: 61);

a V_H CDR2 amino acid sequence as shown in Formula (II):

Glu Ile Asn Pro Asn Asn Gly Arg Ile Asn Xaa_2 Xaa_3 Glu Lys Xaa_4 Lys Thr

(II)

wherein Xaa_2 is Tyr or Gly, Xaa_3 is Asn or Ala and Xaa_4 is Phe or Gly (SEQ ID NO: 62); and

a V_H CDR3 amino acid sequence as shown in Formula (III):

Val Gly Val Xaa_5 Ile Thr Thr Phe Pro Tyr

(III)

wherein Xaa_5 is Met or Ile (SEQ ID NO: 63);

and V_L CDRs having the amino acid sequences shown in SEQ ID NOs: 19, 21 and 23.

10. The isolated antibody of claim 9 wherein Xaa_1 is Met; Xaa_2 is Tyr; Xaa_3 is Asn; Xaa_4 is Phe; and Xaa_5 is Met.

11. The isolated antibody of claim 10 wherein the V_H has the amino acid sequence shown in SEQ ID NO: 45 and the V_L has the amino acid sequence shown in SEQ ID NO: 33.

12. The isolated antibody of claim 9 wherein Xaa_1 is Ile; Xaa_2 is Gly; Xaa_3 is Asn; Xaa_4 is Phe; and Xaa_5 is Met.

13. The isolated antibody of claim 12 wherein the V_H has the amino acid sequence shown in SEQ ID NO: 47 and the V_L has the amino acid sequence shown in SEQ ID NO: 33.

14. The isolated antibody of claim 9 wherein Xaa_1 is Ile; Xaa_2 is Tyr; Xaa_3 is Ala; Xaa_4 is Phe; and Xaa_5 is Met.

15. The isolated antibody of claim 14 wherein the V_H has the amino acid sequence shown in SEQ ID NO: 49 and the V_L has the amino acid sequence shown in SEQ ID NO: 33.

16. The isolated antibody of claim 9 wherein Xaa_1 is Ile; Xaa_2 is Tyr; Xaa_3 is Asn; Xaa_4 is Gly; and Xaa_5 is Met.

17. The isolated antibody of claim 16 wherein the V_H has the amino acid sequence shown in SEQ ID NO: 51 and the V_L has the amino acid sequence shown in SEQ ID NO: 33.

18. The isolated antibody of claim 9 wherein Xaa_1 is Ile; Xaa_2 is Tyr; Xaa_3 is Asn; Xaa_4 is Phe; and Xaa_5 is Ile.

19. The isolated antibody of claim 18 wherein the V_H has the amino acid sequence shown in SEQ ID NO: 53 and the V_L has the amino acid sequence shown in SEQ ID NO: 33.

20. The isolated antibody of claim 9 wherein the V_H has the amino acid sequence shown in SEQ ID NO: 45, 47, 49, 51 or 53 and the V_L has the amino acid sequence shown in SEQ ID NO: 33, 35, 37 or 39.

21. The isolated antibody of claim 4 wherein the antibody is of human origin.

22. The isolated antibody of claim 4 wherein the antibody is of murine origin.

23. The isolated antibody of claim 4 wherein the antibody comprises a Fab fragment.

24. The isolated antibody of claim 4 wherein the antibody comprises a scFv fragment.

25. The isolated antibody of claim 4 wherein the antibody or fragment is human-adapted.

26. The isolated antibody of claim 4 wherein the antibody or fragment comprises a chimeric antibody.

27. The isolated antibody of claim 4 wherein the antibody is conjugated to polyethylene glycol.

28. The isolated antibody of claim 4 wherein the antibody or fragment comprises murine antigen binding residues and human antibody residues.

29. The isolated antibody of claim 4 having an IgG4 isotype.

30. The isolated antibody of claim 29 wherein the Fc domain comprises S228P, P234A and L235A mutations.

31. A pharmaceutical composition comprising the isolated antibody of claim 4 and a pharmaceutically acceptable carrier.

32. An isolated polynucleotide encoding an antibody heavy chain comprising the CDR amino acid sequences shown in SEQ ID NOs: 9, 11 and 13.

33. An isolated polynucleotide encoding an antibody light chain comprising the CDR amino acid sequences shown in SEQ ID NOs: 19, 21 and 23.

34. An isolated polynucleotide encoding an antibody heavy chain comprising the amino acid sequence shown in SEQ ID NO: 6, 25, 27, 29, 31, 45, 47, 49, 51 or 53.

35. The polynucleotide of claim 34 comprising the sequence shown in SEQ ID NO: 5, 26, 28, 30, 32, 46, 48, 50, 52 or 54.

36. An isolated polynucleotide encoding an antibody light chain comprising the amino acid sequence shown in SEQ ID NO: 16, 33, 35, 37 or 39.

37. The polynucleotide of claim 36 comprising the sequence shown in SEQ ID NO: 15, 34, 36, 38 or 40.

38. A vector comprising at least one polynucleotide of claims 32, 33, 34, 35, 36 or 37.

39. A host cell comprising the vector of claim 38.

40. A method of making an antibody reactive with TLR3 comprising culturing the host cell of claim 39 and recovering the antibody produced by the host cell.

41. A hybridoma cell line that produces the antibody of claim 4.

42. A method of inhibiting cellular production of RANTES comprising contacting the isolated antibody of claim 4 with a cell that expresses a TLR3 receptor for a time sufficient to inhibit the production of RANTES.

43. The method of claim 42 wherein the cellular production of IL-6, IL-8 or MIP1-alpha is also inhibited.

44. A method of treating or preventing an inflammatory condition comprising administering a therapeutically effective amount of a TLR3 antagonist to a patient in need thereof for a time sufficient to treat or prevent the inflammatory condition.

45. The method of claim 44 wherein the inflammatory condition is a sepsis-associated condition.

46. The method of claim 44 wherein the inflammatory condition is an inflammatory bowel disease.

47. The method of claim 44 wherein the inflammatory condition is an infection-associated condition.

48. The method of claim 44 wherein the inflammatory condition is an inflammatory pulmonary condition.

49. The method of claim 44 wherein the inflammatory condition is type 2 diabetes, dislipidemia or metabolic syndrome.

50. The method of claim 44 wherein the inflammatory condition is caused by an autoimmune disease.

51. A method of increasing the proliferation rate of a cell comprising contacting a TLR3 antagonist with a cell that expresses a TLR3 receptor for a time sufficient to increase the proliferation rate of the cell.

52. The method of claim 51 wherein the cell is present in the tissue of an animal.

53. The method of claim 51 wherein the cell is an epithelial cell.

54. The method of claim 52 wherein the tissue is colonic tissue.

55. The method of claim 52 wherein the tissue exhibits a pathology associated with an inflammatory condition.

56. The method of claim 55 wherein the inflammatory condition is an inflammatory bowel disease.

57. A method of treating or preventing a condition resulting from cell death comprising administering a therapeutically effective amount of a TLR3 antagonist to a patient in need thereof for a time sufficient to treat the condition.

58. The method of claim 44, 51 or 57 wherein the TLR3 antagonist is an isolated antibody reactive with TLR3 having the antigen binding ability of a monoclonal antibody comprising the amino acid sequences of the heavy chain CDRs as shown in SEQ ID

NOs: 9, 11 and 13 and the amino acid sequences of the light chain CDRs as shown in SEQ ID NOs: 19, 21 and 23.

59. The method of claim 58 wherein the isolated antibody reactive with TLR3 comprises the amino acid sequences of the heavy chain CDRs as shown in SEQ ID NOs: 9, 11 and 13 and the amino acid sequences of the light chain CDRs as shown in SEQ ID NOs: 19, 21 and 23.

60. The method of claim 59 wherein the isolated antibody comprises a V_H having the amino acid sequence shown in SEQ ID NO: 6, 25, 27, 29 or 31 and a V_L having the amino acid sequence shown in SEQ ID NO: 16, 33, 35, 37 or 39.

61. The method of claim 44, 51 or 57 wherein the TLR3 antagonist is an isolated antibody reactive with TLR3 having the antigen binding ability of a monoclonal antibody comprising a V_H having the amino acid sequence shown in SEQ ID NO: 45, 47, 49, 51 or 53 and a V_L having the amino acid sequence shown in SEQ ID NO: 33, 35, 37 or 39.

CLAIMS

[Claim 1]

An isolated antibody reactive with TLR3 and including a heavy chain variable region (V_H) possessing an amino acid sequence expressed by SEQ ID NO: 6 and a light chain variable region (V_L) possessing the amino acid sequence expressed by SEQ ID NO: 16.

[Claim 2]

An isolated antibody reactive with TLR3 and including a V_H possessing the amino acid sequence expressed by SEQ ID NO: 25 and the V_L amino acid sequence expressed by SEQ ID NO: 33.

[Claim 3]

The isolated antibody set forth by Claim 1 or 2, wherein the antibody is of human origin.

[Claim 4]

The isolated antibody set forth by any of Claims 1 through 3, wherein the antibody includes a Fab fragment.

[Claim 5]

The isolated antibody set forth by any of Claims 1 through 3, wherein the antibody is coupled with polyethylene glycol.

[Claim 6]

The isolated antibody set forth by any of Claims 1 through 3 including an IgG4 isotype.

[Claim 7]

A pharmaceutical composition including the isolated antibody set forth by any of Claims 1 through 3 and a pharmaceutically permissible carrier.

[Claim 8]

A pharmaceutical preparation provided for enhancing the breeding ratio of a cell expressing a TLR3 receptor and including a TLR3 antagonist as an effective component, the TLR3 antagonist being the antibody set forth by any of Claims 1 through 3.

[Claim 9]

The preparation set forth by Claim 8, wherein the TLR3 antagonist is the antibody set forth by Claim 1.

[Claim 10]

The preparation set forth by Claim 8 or 9, wherein the cell exists within an animal tissue.

[Claim 11]

The preparation set forth by Claim 8 or 9, wherein the cell is an epithelial cell.

[Claim 12]

The preparation set forth by Claim 10, wherein the tissue is a rectal tissue.

[Claim 13]

The preparation set forth by Claim 10, wherein the tissue manifests a pathology accompanying an inflammatory state.

[Claim 14]

The preparation set forth by Claim 13, wherein the inflammatory state is inflammatory enteropathy.