

We claim:

1. An isolated recombinant antibody or antigen-binding fragment thereof that specifically binds to *P. aeruginosa* PcrV, wherein the antibody or antigen-binding fragment thereof has one or more of the following characteristics:

(a) comprises three heavy chain complementarity determining regions (CDRs) (HCDR1, HCDR2 and HCDR3) contained within any one of the heavy chain variable region (HCVR) sequences selected from the group consisting of SEQ ID NOs: 34, 50, 2, and 18; and three light chain CDRs (LCDR1, LCDR2 and LCDR3) contained within any one of the light chain variable region (LCVR) sequences selected from the group consisting of SEQ ID NOs: 42, 58, 10, and 26;

(b) is a fully human monoclonal antibody;

(c) binds to full length PcrV with a dissociation constant (K_D) of less than 10^{-8} M, as measured in a surface plasmon resonance assay at 25°C;

(d) binds to full length PcrV with a dissociation constant (K_D) of less than 10^{-8} M, as measured in a surface plasmon resonance assay at 37°C;

(e) demonstrates neutralization of *P. aeruginosa* strain 6077 with an IC_{50} ranging from about 10^{-11} M to about 10^{-8} M in a cytotoxicity assay;

(f) demonstrates neutralization of *P. aeruginosa* strain ATCC 700888 with an IC_{50} ranging from about 10^{-9} M to about 10^{-7} M in a cytotoxicity assay;

(g) demonstrates neutralization of *P. aeruginosa* strain 6077 with an IC_{50} ranging from about 10^{-10} M to about 10^{-6} M in a hemolytic assay;

(h) demonstrates neutralization of *P. aeruginosa* strain ATCC 700888 with an IC_{50} ranging from about 10^{-10} M to about 10^{-7} M in a hemolytic assay;

(i) decreases mortality from *P. aeruginosa* strain 6206 or strain 6077 in mice treated prophylactically with 5 mg/kg relative to untreated mice in an acute pneumonia model;

(j) decreases mortality from *P. aeruginosa* strain 6206 or strain 6077 in mice treated prophylactically with 1.0, 0.2 or 0.04 mg/kg relative to untreated mice in an acute pneumonia model;

(k) decreases lung bacterial burden of *P. aeruginosa* strain 6206 in mice treated prophylactically at 0.1 mg/kg or 0.2 mg/kg relative to untreated mice in an acute pneumonia model;

(l) decreases lung bacterial burden of *P. aeruginosa* strain PA01 in mice treated prophylactically at 25 mg/kg relative to untreated mice in an acute pneumonia model; and/or

(m) cross-competes with a reference antibody, wherein the reference antibody comprises a heavy chain variable region (HCVR) and a light chain variable region (LCVR) amino acid sequence selected from the group consisting of any of the HCVR and LCVR amino acid sequences of Table 1.

2. An isolated recombinant antibody or antigen-binding fragment thereof that specifically binds to *P. aeruginosa* PcrV, wherein the antibody or antigen-binding fragment thereof has one or more of the following characteristics:

(a) comprises three heavy chain complementarity determining regions (CDRs) (HCDR1, HCDR2 and HCDR3) contained within any one of the heavy chain variable region (HCVR) sequences selected from the group consisting of SEQ ID NOs: 34, 50, 2, and 18; and three light chain CDRs (LCDR1, LCDR2 and LCDR3) contained within any one of the light chain variable region (LCVR) sequences selected from the group consisting of SEQ ID NOs: 42, 58, 10, and 26;

(b) binds to full length PcrV with an EC_{50} of less than about $10^{-8}M$;

(c) binds to PcrV 136-233 (SEQ ID NO: 81) with an EC_{50} of less than about $10^{-8}M$;

(d) interacts with at least one amino acid sequence selected from the group consisting of (i) amino acid residues ranging from about position 150 to about position 170 of SEQ ID NO: 78 and (ii) amino acid residues ranging from about position 155 to about 170 of SEQ ID NO: 78; and/or

(e) interacts with at least one amino acid sequence selected from the group consisting of SEQ ID NO: 85 and SEQ ID NO: 86.

3. The isolated antibody or antigen-binding fragment thereof of either claim 1 or 2, comprising an HCVR having an amino acid sequence selected from the group consisting of SEQ ID NOs: 34, 50, 2, and 18.

4. The isolated antibody or antigen-binding fragment thereof of any one of claims 1-3, comprising an LCVR having an amino acid sequence selected from the group consisting of SEQ ID NOs: 42, 58, 10, and 26.

5. The isolated antibody or antigen-binding fragment thereof of any one of claims 1 – 4, comprising:

- (a) an HCDR1 domain having an amino acid sequence selected from the group consisting of SEQ ID NOs: 36, 52, 4, and 20;
- (b) an HCDR2 domain having an amino acid sequence selected from the group consisting of SEQ ID NOs: 38, 54, 6, and 22;
- (c) an HCDR3 domain having an amino acid sequence selected from the group consisting of SEQ ID NOs: 40, 56, 8, and 24;
- (d) an LCDR1 domain having an amino acid sequence selected from the group consisting of SEQ ID NOs: 44, 60, 12, and 28;
- (e) an LCDR2 domain having an amino acid sequence selected from the group consisting of SEQ ID NOs: 46, 62, 14, and 30; and
- (f) an LCDR3 domain having an amino acid sequence selected from the group consisting of SEQ ID NOs: 48, 64, 16, and 32.

6. The isolated antibody or antigen-binding fragment of any one of claims 1 – 5, comprising an HCVR/LCVR amino acid sequence pair selected from the group consisting of SEQ ID NOs: 34/42, 50/58, 2/10, and 18/26.

7. The isolated antibody or antigen-binding fragment of claim 6, comprising an HCVR/LCVR amino acid sequence pair selected from the group consisting of SEQ ID NOs: 34/42 and 50/58.

8. The isolated antibody or antigen-binding fragment thereof of any one of claims 1 – 7, comprising an HCDR1 amino acid sequence of SEQ ID NO: 36; an HCDR2 amino acid sequence of SEQ ID NO: 38; an HCDR3 amino acid sequence of SEQ ID NO: 40; an LCDR1 amino acid sequence of SEQ ID NO: 44; an LCDR2 amino acid sequence of SEQ ID NO: 46; and an LCDR3 amino acid sequence of SEQ ID NO: 48.

9. The isolated antibody or antigen-binding fragment thereof of any one of claims 1 – 7, comprising an HCDR1 amino acid sequence of SEQ ID NO: 52; an HCDR2 amino acid sequence of SEQ ID NO: 54; an HCDR3 amino acid sequence of SEQ ID NO: 56; an LCDR1 amino acid sequence of SEQ ID NO: 60; an LCDR2 amino acid sequence of SEQ ID NO: 62 and an LCDR3 amino acid sequence of SEQ ID NO: 64.

10. The isolated antibody or antigen-binding fragment thereof of any one of claims 1 – 7, comprising an HCDR1 amino acid sequence of SEQ ID NO: 4; an HCDR2 amino acid sequence of SEQ ID NO: 6; an HCDR3 amino acid sequence of SEQ ID NO: 8; an LCDR1 amino acid sequence of SEQ ID NO: 12; an LCDR2 amino acid sequence of SEQ ID NO: 14; and an LCDR3 amino acid sequence of SEQ ID NO: 16.

11. The isolated antibody or antigen-binding fragment thereof of any one of claims 1 – 7, comprising an HCDR1 amino acid sequence of SEQ ID NO: 20; an HCDR2 amino acid sequence of SEQ ID NO: 22; an HCDR3 amino acid sequence of SEQ ID NO: 24; an LCDR1 amino acid sequence of SEQ ID NO: 28; an LCDR2 amino acid sequence of SEQ ID NO: 30; and an LCDR3 amino acid sequence of SEQ ID NO: 32.

12. An isolated monoclonal antibody or antigen-binding fragment thereof that competes for binding to PcrV with a reference antibody or antigen-binding fragment comprising the CDRs of a HCVR, wherein the HCVR has an amino acid sequence selected from the group consisting of SEQ ID NOs: 34, 50, 2, and 18; and the CDRs of a LCVR, wherein the LCVR has an amino acid sequence selected from the group consisting of SEQ ID NOs: 42, 58, 10, and 26.

13. The isolated antibody or antigen-binding fragment thereof of claim 12, wherein the antibody or antigen-binding fragment thereof competes for binding to PcrV 136-233 (SEQ ID NO: 81) with the reference antibody or antigen-binding fragment thereof.

14. An isolated monoclonal antibody or antigen-binding fragment thereof that binds to the same epitope on PcrV as a reference antibody or antigen-binding fragment comprising the CDRs of a HCVR, wherein the HCVR comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 34, 50, 2, and 18; and the CDRs of a LCVR, wherein the LCVR comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 42, 58, 10, and 26.

15. A method of neutralizing *P. aeruginosa*, the method comprising exposing a cell infected with *P. aeruginosa* to a composition comprising one or more anti-PcrV antibodies or antigen-binding fragments thereof according to any one of claims 1-14, wherein the exposing results in enhanced protection from cell death.

16. The method of claim 15, wherein the *P. aeruginosa* is neutralized *in vitro* or *in vivo*.

17. The method of claim 15, wherein the enhanced protection is observed when the antibody is used alone, or when it is used in combination with one or more additional therapeutic agents or antibodies against *P. aeruginosa*.

18. The method of claim 17, wherein the one or more additional therapeutic agents is selected from the group consisting of an antibiotic, an anti-inflammatory drug, a different antibody to *P. aeruginosa*, and a therapeutic useful for treating a co-infection.

19. The method of claim 18, wherein the one or more additional therapeutic agents is a therapeutic useful for treating a co-infection and wherein the co-infection is a *S. aureus* infection.

20. The method of claim 17, wherein the one or more additional therapeutic agents is a different anti-*P. aeruginosa* antibody.

21. A pharmaceutical composition comprising one or more isolated antibodies or antigen-binding fragments thereof according to any one of claims 1 – 14 and a pharmaceutically acceptable carrier or diluent.

22. The pharmaceutical composition of claim 21, wherein the one or more isolated antibodies or antigen-binding fragments thereof comprise three HCDRs and three LCDRs within an HCVR/LCVR amino acid sequence pair selected from the group consisting SEQ ID NOs: 34/42, 50/58, 2/10, and 18/26.

23. The pharmaceutical composition of claim 21, wherein the one or more isolated antibodies or antigen-binding fragments thereof comprise the HCVR/LCVR amino acid sequence pair selected from the group consisting SEQ ID NOs: 34/42, 50/58, 2/10, and 18/26.

24. The pharmaceutical composition of claim 23, wherein the one or more isolated antibodies or antigen-binding fragments thereof comprise the HCVR/LCVR amino acid sequence pair is selected from the group consisting of SEQ ID NOs: 34/42 and 50/58.

25. The pharmaceutical composition of claim 21, wherein the isolated antibody or an antigen-binding fragment thereof comprises an HCDR1 amino acid sequence of SEQ ID NO: 36; an HCDR2 amino acid sequence of SEQ ID NO: 38; an HCDR3 amino acid sequence of SEQ ID NO: 40; an LCDR1 amino acid sequence of SEQ ID NO: 44; an LCDR2 amino acid sequence of SEQ ID NO: 46; and an LCDR3 amino acid sequence of SEQ ID NO: 48.

26. The pharmaceutical composition of claim 21, wherein the isolated antibody or an antigen-binding fragment thereof comprises an HCDR1 amino acid sequence of SEQ ID NO: 52; an HCDR2 amino acid sequence of SEQ ID NO: 54; an HCDR3 amino acid sequence of SEQ ID NO: 56; an LCDR1 amino acid sequence of SEQ ID NO: 60; an LCDR2 amino acid sequence of SEQ ID NO: 62 and an LCDR3 amino acid sequence of SEQ ID NO: 64.

27. The pharmaceutical composition of claim 21, wherein the isolated antibody or an antigen-binding fragment thereof comprises an HCDR1 amino acid sequence of SEQ ID NO: 4; an HCDR2 amino acid sequence of SEQ ID NO: 6; an HCDR3 amino acid sequence of SEQ ID NO: 8; an LCDR1 amino acid sequence of SEQ ID NO: 12; an LCDR2 amino acid sequence of SEQ ID NO: 14; and an LCDR3 amino acid sequence of SEQ ID NO: 16.

28. The pharmaceutical composition of claim 21, wherein the isolated antibody or an antigen-binding fragment thereof comprises an HCDR1 amino acid sequence of SEQ ID NO: 20; an HCDR2 amino acid sequence of SEQ ID NO: 22; an HCDR3 amino acid sequence of SEQ ID NO: 24; an LCDR1 amino acid sequence of SEQ ID NO: 28; an LCDR2 amino acid sequence of SEQ ID NO: 30; and an LCDR3 amino acid sequence of SEQ ID NO: 32.

29. An isolated polynucleotide molecule comprising a polynucleotide sequence that encodes an HCVR and/or an LCVR of an antibody as set forth in any one of claims 1 – 14.

30. A vector comprising the polynucleotide sequence of claim 29.

31. A cell expressing the vector of claim 30.

32. A method of decreasing the risk of acquiring *P. aeruginosa* infection, the method comprising administering an antibody or antigen-binding fragment thereof of any one of claims 1-14, or a pharmaceutical composition of claims 21-28, to a subject at greater risk for *P. aeruginosa* infection.

33. The method of claim 32, wherein the subject at greater risk for *P. aeruginosa* infection is selected from the group consisting of a subject undergoing surgery, a subject being treated for a major illness, a trauma patient, an intravenous drug user, a subject having severe burns, a subject using a breathing machine, a subject with a catheter, a subject undergoing chemotherapy, a subject having diabetes, a subject with cystic fibrosis, a subject with tuberculosis, a subject with HIV, or a subject with a compromised immune system.

34. A method of decreasing bacterial load in a subject with a *P. aeruginosa* infection, the method comprising administering to the subject an antibody or antigen-binding fragment thereof of any one of claims 1-14, or a pharmaceutical composition of claims 21-28, to the subject.

35. A method of increasing the survival, or the likelihood of survival of a subject suffering from infection with *P. aeruginosa*, or a subject at risk for *P. aeruginosa* infection, the method comprising administering an antibody or antigen-binding fragment thereof of any one of claims 1-14, or a pharmaceutical composition of claims 21-28 to the subject.

36. A method of ameliorating or reducing the severity, duration, or frequency of occurrence, of at least one symptom of a *P. aeruginosa* infection, the method comprising administering an antibody or antigen-binding fragment thereof of any one of claims 1-14, or a pharmaceutical composition of claims 21-28, to a subject in need thereof.

37. The method of claim 36, wherein the at least one symptom is selected from the group consisting of fever, chills, headache, fatigue, joint pain, stiffness, myalgia, diarrhea, vomiting, pain, itching, liquid discharge in the ears, rashes, pus-filled pimples on the skin, eye pain, redness in an eye, pneumonia, coughing, congestion, soft tissue discharge of green pus, sweet, fruity smell, and urinary tract infection.

38. The method of claim 36, wherein the pharmaceutical composition is administered prophylactically or therapeutically to the subject in need thereof.

39. The method of claim 36, wherein the subject is selected from the group consisting of a subject undergoing surgery, a subject being treated for a major illness, a trauma patient, an intravenous drug user, a subject having severe burns, a subject using a breathing machine, a subject with a catheter, a subject undergoing chemotherapy, a subject having diabetes, a subject with cystic fibrosis, a subject with tuberculosis, a subject with HIV, or a subject with a compromised immune system.

40. The method of claim 36, wherein the subject in need thereof has a *P. aeruginosa* infection.

41. The method of claim 36, wherein the subject is at risk of contracting a *P. aeruginosa* infection.

42. The method of claim 40, wherein the subject has a *S. aureus* infection.

43. The method of any one of claims 32 – 42, wherein the antibody or antigen-binding fragment thereof, or the pharmaceutical composition comprising the antibody or antigen-binding fragment thereof, is administered in combination with a second therapeutic agent.

44. The method of claim 43, wherein the second therapeutic agent is selected from the group consisting of an antibiotic, an anti-inflammatory drug (e.g. corticosteroids and non-steroidal anti-inflammatory drugs), and a different antibody to *P. aeruginosa*.

45. The method of any one of claims 32 - 42, wherein the antibody or antigen-binding fragment thereof, or the pharmaceutical composition comprising the antibody or antigen-binding fragment thereof, is administered subcutaneously, intravenously, intradermally, intramuscularly, intranasally, or orally.

46. The method of claim 40, wherein the subject has pneumonia, bacteremia, a bone infection, a joint infection, a skin infection, a burn infection, a wound infection, or any combination thereof.

47. The method of claim 40, wherein the *P. aeruginosa* is resistant or partially resistant to an antibiotic.

48. A method of increasing survival, or the likelihood of survival of a subject suffering from cystic fibrosis, the method comprising administering at least one antibody or antigen-binding fragment of any one of claims 1 – 14, or a pharmaceutical composition of any of claims 21 - 28 to a subject in need thereof.

49. The method of claim 48, wherein the subject does not have pneumonia symptoms at the time of administration.