

Claims

1. A method for the removal of a pathogen from blood or a blood product comprising red blood cells, said method comprising:
- 5 - separating said blood or blood product into at least two components, a first component comprising red blood cells (RBCs) and substantially free of white blood cells (WBCs) and platelets and a second component comprising WBCs and platelets and substantially free of RBCs;
- contacting said first component with a filter comprising a non-specific RBC
- 10 adhesion molecule binder thereby depleting said first component of RBCs that have bound at least one pathogen;
- optionally combining said first component that is depleted of RBCs that have bound at least one pathogen and said second component.
- 15 2. Method according to claim 1, further comprising storing said first component that is depleted of RBCs that have bound at least one pathogen and said second component.
3. A method for the removal of a pathogen from blood of a patient in need
- 20 thereof comprising:
- withdrawing blood from said patient;
- separating said blood into at least two blood components, a first component comprising red blood cells (RBCs) and substantially free of white blood cells (WBCs) and platelets and a second component comprising WBCs and platelets and
- 25 substantially free of RBCs;
- contacting said first component with a filter comprising a non-specific RBC adhesion molecule binder thereby depleting said first component of RBCs that have bound at least one pathogen;
- optionally combining said first component that is depleted of RBCs that have
- 30 bound at least one pathogen and said second component;
- returning said first component that is depleted of RBCs that have bound at least one pathogen and said second component to said patient.
4. Method according to claim 3 for the treatment of sepsis in a patient in need
- 35 thereof.

5. Method according to claim 3 or 4, wherein said blood is continuously withdrawn from said patient and said first component that is depleted of RBCs that have bound at least one pathogen and said second component are continuously returned to said patient.
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6. A non-specific red blood cell (RBC) adhesion molecule binder for use in a treatment of removing a pathogen from blood of a subject, said treatment comprising contacting a blood component comprising red blood cells (RBCs) and substantially free of white blood cells (WBCs) and platelets with a filter comprising
- 10 said non-specific RBC adhesion molecule binder to allow binding of RBCs that have bound at least one pathogen to said non-specific RBC adhesion molecule binder, thereby removing said RBCs that have bound at least one pathogen from said blood component.
- 15 7. A non-specific RBC adhesion molecule binder according to claim 6 for use in the treatment of sepsis or a developing sepsis.
8. A non-specific RBC adhesion molecule binder according to claim 6 or 7, wherein said treatment comprises separating said blood into at least two blood
- 20 components, a first component comprising red blood cells (RBCs) and substantially free of white blood cells (WBCs) and platelets and a second component comprising WBCs and platelets and substantially free of RBCs.
9. A method or non-specific RBC adhesion molecule binder for use according to
- 25 any one of claims 1-8, wherein said non-specific RBC adhesion molecule binder is a polymer.
10. A method or non-specific RBC adhesion molecule binder for use according to any one of claims 1-9, wherein said pathogen is a bacterium, a virus, a parasite or a
- 30 fungus, preferably a bacterium or a fungus, more preferably selected from the group consisting of *Staphylococcus aureus*, *Salmonella typhimurium*, *Escherichia coli*, *Candida albicans*, *Enterococcus faecalis* and *Bacillus subtilis*.
11. A system (1) for removing a pathogen from blood or a blood product,
- 35 comprising:

- a separation device (2), preferably comprising a centrifuge, for separating said blood or said blood product into at least a first component comprising red blood cells (RBCs) and being substantially free of white blood cells (WBCs) and platelets and a second component comprising white blood cells (WBCs) and platelets and
5 being substantially free of red blood cells (RBCs);
 - a filter device (3) for depleting said first component substantially of RBCs that have bound at least one pathogen, said filter device comprising a non-specific RBC adhesion molecule binder, wherein said non-specific RBC adhesion molecule binder preferably is a polymer;
 - 10 - a conduit (4) for conducting said first component from the separation device (2), e.g. from a first outlet thereof (2b), to the filter device (3), e.g. to an inlet thereof (3a);
 - an outlet conduit (10) for conducting the filtered first component, which is substantially depleted of RBCs that have bound at least one pathogen, away from
15 said filter device (3), wherein the system (1) is arranged to feed the filtered first component, which is substantially depleted of RBCs that have bound at least one pathogen, to a subject (9) and/or to an administering device (6b) for administering at least said filtered first component to a subject (9) .
- 20 12. A system (1) according to claim 11 further comprising:
- a second component outlet conduit (11) for conducting the separated second component away from the separation device (2), said second component outlet conduit (11) being in fluid connection with a second outlet (2c) of the separation device (2) for letting the second component out of the separation device (2),
25 wherein the system (1) is arranged to put the filtered first component and at least part of the second component of the blood or blood product together in order to obtain a blood or blood product substantially free of pathogens, or at least substantially free of RBC bound pathogens.
- 30 13. A system (1) according to claim 12, wherein the outlet conduit (10) for conducting the filtered first component away from the filter device (3) merges with the second component outlet conduit (11), such that the filtered first component and the second component can join, and can preferably mix.

14. A system (1) according to claim 12, further comprising a mixing chamber (12) or another mixing unit (12) for mixing said second component with said filtered first component.
- 5 15. A system (1) according to any one of claims 11-13, further comprising an anticoagulant supply unit (8) for adding an anticoagulant to the blood or the blood product, wherein said anticoagulant supply unit (8) is preferably situated upstream of the separation device (2), and more preferably is arranged for feeding the anticoagulant into a supply conduit (5) for supplying the blood or blood product to
10 the separation device (2).
16. An apparatus for removing a pathogen from blood or a blood product comprising a housing (15) and a system (1) according to any one of claims 11-15.
- 15 17. A pathogen bound RBC filter device for use in a system according to any one of claims 11-15, wherein said pathogen bound RBC filter device is arranged for depleting a blood product substantially of RBCs that have bound at least one pathogen, said filter device comprising a non-specific RBC adhesion molecule binder, preferably wherein said non-specific RBC adhesion molecule binder is a
20 polymer.
18. A method for detecting pathogens in a sample of blood or of a blood product comprising red blood cells (RBCs), the method comprising:
i) contacting said sample with a support comprising a non-specific RBC adhesion
25 molecule binder to allow binding of RBCs that have bound at least one pathogen to said binder;
ii) detecting the presence of RBCs that have bound at least one pathogen.
19. The method according to claim 18 further comprising separating said
30 sample into at least two components prior to step i), a first component comprising red blood cells (RBCs) and substantially free of white blood cells (WBCs) and platelets and a second component comprising WBCs and platelets and substantially free of RBCs, wherein step i) comprising contacting said first component of said sample with a support comprising a non-specific RBC adhesion

molecule binder thereby to allow binding of said RBCs that have bound at least one pathogen to said binder.

20. The method according to claim 18 or 19 further comprising isolating
5 RBCs that are bound to said support from said sample, preferably by removing cells and other components in said sample that have not bound to said binder.

21. The method according to claim 20, further comprising lysing said RBCs that are bound to said support following said isolation step.

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22. The method according to any one of claims 18-21, further comprising determining at least one characteristic of said pathogens if RBCs that have bound at least one pathogen are detected in said sample, wherein said characteristic is selected from the group consisting of the type of pathogen, gram-positivity or gram-
15 negativity if said pathogen is a bacterium, drug or antibiotic resistance of the pathogens, and the identity of the pathogens.

23. The method according to any one of claims 18-22, wherein said support comprises beads coated with said non-specific RBC adhesion molecule binder,
20 preferably a polymer or mixture of two or more polymers.

24. The method according to any one of claims 18-23 wherein said detecting step and/or said determining step are carried out by flow cytometry.

25. The method according to any one of claims 18-24 wherein said sample is a sample from an individual having an infectious pathogen in the blood, an individual suspected of having an infectious pathogen in the blood, an individual suffering from sepsis, an individual suspected of suffering from sepsis, an individual at risk of suffering from sepsis.

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26. A method for identifying pathogens in a sample of blood or of a blood product comprising red blood cells (RBCs), the method comprising:

- i) contacting said sample with a support comprising a non-specific RBC adhesion molecule binder to allow binding of RBCs that have bound at least one pathogen to said binder;
- ii) isolating RBCs that are bound to said support from said sample, preferably by removing cells and other components in said sample that have not bound to said binder;
- iii) identifying the pathogen that is bound to said RBCs bound to said support.

27. A method for diagnosing an infection in the blood of a patient, , the method comprising detecting pathogens and/or identifying pathogens in a sample of blood or a blood product comprising red blood cells (RBCs) of said patient with a method according to any one of claims 18-26.

28. A method for isolating and/or enriching pathogens from a sample of blood or of a blood product comprising red blood cells (RBCs), the method comprising:
i) contacting said sample with a support comprising a non-specific RBC adhesion molecule binder to allow binding of RBCs that have bound at least one pathogen to said binder;
ii) isolating RBCs that are bound to said support from said sample, preferably by removing cells and other components in said sample that have not bound to said binder.

29. A method for determining susceptibility for antibiotics of a pathogen, the method comprising,
- detecting pathogens and/or identifying pathogens in a sample of blood or a blood product comprising red blood cells (RBCs) with a method according to any one of claims 18-26;
- isolating RBCs that are bound to said support from said sample;
- contacting said isolated RBCs that are bound to said support with one or more antibiotic agents; and
- determining the growth of a functional activity of the pathogen.

30. A method for determining the presence of pathogens in a whole blood sample of an individual suspected of having an infectious pathogen in the blood, suffering from sepsis, suspected of suffering from sepsis or at risk of developing sepsis, the method comprising detecting the presence of red blood cells (RBCs) that
5 have bound at least one pathogen using cytometry or microscopy.

31. The method according to claim 30, wherein said detecting step is carried out by flow cytometry whereby RBCs that have bound at least one pathogen are detected by cell sorting for RBCs and labelling of pathogens.
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32. The method according to claim 31, wherein said labelling of pathogens comprises DNA labelling.

33. The method according to claim 31, wherein the method comprises
15 determining the presence of bacteria and said labelling comprises labelling with a general bacteria label.

34. The method according to any one of claims 30-33, wherein said individual is suspected of having an infectious pathogen in the blood, suspected of suffering
20 from sepsis or at risk of developing sepsis.