

CLAIMS

1. A method of monitoring the progress of a disease in a subject suffering from an infection, comprising:
 - (i) contacting a body fluid sample obtained from the subject with a binding agent to detect or measure the level of cell free nucleosomes or a component thereof;
 - (ii) repeating step (i) on one or more occasions; and
 - (iii) using any changes in the level of cell free nucleosomes or component thereof to monitor the progression of the infection in the subject.
2. A method of assigning a risk of an adverse outcome to a subject suffering from an infection, comprising:
 - (i) contacting a body fluid sample obtained from the subject with a binding agent to detect or measure the level of cell free nucleosomes or a component thereof; and
 - (ii) using the level of cell free nucleosomes detected to assign the likelihood of an adverse outcome to said subject,wherein a subject identified with a high likelihood of an adverse outcome is assigned for medical intervention.
3. The method as defined in claim 1 or claim 2, wherein the infection is a viral, bacterial, fungal or microbial infection.
4. The method as defined in any one of claims 1 to 3, wherein the infection is a respiratory tract infection.
5. The method as defined in claim 4, wherein the respiratory tract infection is selected from: influenza, pneumonia and severe acute respiratory syndrome (SARS).
6. The method as defined in claim 1 or claim 2, wherein the subject is suffering from sepsis or septic shock.
7. The method as defined in any one of claims 1 to 6, wherein the body fluid sample is a blood, serum or plasma sample.
8. The method as defined in any one of claims 1 to 7, wherein the cell free nucleosome is a part of, or derived from, a neutrophil extracellular trap.

9. The method as defined in any one of claims 1 to 8, wherein the component of the cell free nucleosome comprises an epigenetic feature of the cell free nucleosome.
10. The method as defined in claim 9, wherein the epigenetic feature is a histone isoform, such as a histone isoform of a core nucleosome, in particular a histone H3 isoform.
11. The method as defined in claim 10, wherein the histone isoform is H3.1.
12. The method as defined in claim 9, wherein the epigenetic feature is a histone post translational modification (PTM), such as a histone PTM of a core nucleosome, in particular a histone H3 or H4 PTM.
13. The method as defined in claim 12, wherein the histone PTM is selected from citrullination or ribosylation.
14. The method as defined in any one of claims 1 to 13, wherein the level of cell free nucleosomes or component thereof is detected or measured using an immunoassay, immunochemical, mass spectroscopy, chromatographic, chromatin immunoprecipitation or biosensor method.
15. The method as defined in any one of claims 1 to 14, wherein the method of detection or measurement comprises contacting the body fluid sample with a solid phase comprising a binding agent that detects cell free nucleosomes or a component thereof, and detecting binding to said binding agent.
16. The method as defined in any one of claims 1 to 15, wherein the method of detection or measurement comprises: (i) contacting the sample with a first binding agent which binds to an epigenetic feature of a cell free nucleosome; (ii) contacting the sample bound by the first binding agent in step (i) with a second binding agent which binds to cell free nucleosomes; and (iii) detecting or quantifying the binding of the second binding agent in the sample.
17. The method as defined in any one of claims 1 to 16, wherein the subject is a human or an animal subject.
18. The method as defined in any one of claims 1 to 17, additionally comprising comparing the level of cell free nucleosomes or component thereof in the body fluid sample of the subject with one or more controls.

19. The method as defined in claim 18, wherein the control is a healthy subject.
20. The method as defined in claim 18, wherein the control is a subject with the infection displaying no, or mild, symptoms.
21. The method as defined in any one of claims 1 to 20, wherein the level of cell free nucleosomes or component thereof is elevated compared to the control.
22. The method as defined in any one of claims 1 to 21, wherein the level of cell free nucleosomes is detected or measured as one of a panel of measurements.
23. The method as defined in claim 22, wherein the panel comprises one or more interleukins.
24. The method as defined in claim 23, wherein the one or more interleukins are selected from the group consisting of: IL-6 and IL-12.
25. The method as defined in any one of claims 22 to 24, wherein the panel comprises C reactive protein (CRP), myeloperoxidase (MPO), D-Dimer and/or factor VII-activating protease (FSAP).
26. The method as defined in any one of claims 22 to 25, wherein the panel comprises MPO.
27. A method of detecting a subject in need of medical treatment for pneumonia, acute respiratory syndrome (ARS), acute respiratory distress syndrome (ARDS) or severe acute respiratory syndrome (SARS), comprising:
- (i) contacting a body fluid sample obtained from the subject with a binding agent to detect or measure the level of cell free nucleosomes or a component thereof; and
 - (ii) using the level of cell free nucleosomes as an indicator that the subject is in need of medical treatment for pneumonia, ARS, ARDS or SARS.
28. A method of detecting a subject in need of medical treatment for sepsis or septic shock, comprising:
- (i) contacting a body fluid sample obtained from the subject with a binding agent to detect or measure the level of cell free nucleosomes or a component thereof; and

(ii) using the level of cell free nucleosomes as an indicator that the subject is in need of medical treatment for sepsis or septic shock.

29. A method of treating a NETosis related disease comprising the administration of a therapeutic antibody directed to bind to a nucleosome or component thereof, myeloperoxidase, neutrophil elastase or C-reactive protein.

30. The method as defined in claim 29, wherein the NETosis related disease involves high levels of neutrophil extracellular traps.

31. The method as defined in claim 29 or claim 30, wherein the NETosis related disease is a viral or bacterial infection.

32. The method as defined in any one of claims 29 to 31, wherein the therapeutic antibody is directed to bind to an epitope present in intact nucleosomes.

33. The method as defined in any one of claims 29 to 31, wherein the therapeutic antibody is directed to bind to an epitope present in a clipped nucleosome.

34. The method as defined in any one of claims 29 to 33, wherein the therapeutic antibody is directed to bind to a component of the nucleosome which is histone H3.1 or a citrullinated histone.

35. The method as defined in any one of claims 29 to 34, wherein the therapeutic antibody is directed to bind to a histone H3.1 epitope located at amino acid position 30-33 in the amino acid sequence of histone H3.1.