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~~ such as a respiratory tract infection ~~is~~ selected from: influenza, pneumonia and severe acute respiratory syndrome (SARS).

~~6~~4. The method as defined in claim 1 or claim 2, wherein the subject is suffering from sepsis or septic shock.

~~7~~5. The method as defined in any one of claims 1 to 4~~6~~, wherein the body fluid sample is a blood, serum or plasma sample.

~~8~~6. The method as defined in any one of claims 1 to 5~~7~~, wherein the cell free nucleosome is a part of, or derived from, a neutrophil extracellular trap.

~~9~~7. The method as defined in any one of claims 1 to 6~~8~~, wherein the component of the cell free nucleosome comprises an epigenetic feature of the cell free nucleosome.

~~10~~8. The method as defined in claim 7~~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~~ or 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~~9. The method as defined in any one of claims 1 to 8~~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.

10~~5~~. The method as defined in any one of claims 1 to 9~~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.

11~~6~~. The method as defined in any one of claims 1 to 10~~5~~, 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.

12~~7~~. The method as defined in any one of claims 1 to 11~~6~~, wherein the subject is a human or an animal subject.

13~~8~~. The method as defined in any one of claims 1 to 12~~7~~, 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,~~ optionally wherein the control is a healthy subject~~.~~

~~20. The method as defined in claim 18, wherein the control is~~ or 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~~14. The method as defined in any one of claims 1 to ~~2~~13, 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~~15. 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~~16. 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~~17. ~~A method of treating a NETosis related disease comprising the administration~~ Use of a therapeutic antibody directed to bind to a nucleosome or component thereof, myeloperoxidase, neutrophil elastase or C-reactive protein, for the manufacture of a medicament for the treatment of a NETosis related disease.

~~30~~18. The ~~method~~ use as defined in claim ~~29~~17, 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~~ such as a viral or bacterial infection.

~~32~~19. The ~~method~~ use as defined in ~~any one of~~ claim~~s 29 to 31~~17 or claim 18, 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~~ or a clipped nucleosome.

~~34~~20. The ~~method~~ use as defined in any one of claims ~~29~~17 to ~~33~~19, 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,~~ optionally 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.