CLAIMS

1. A method of detecting a cell free chromatin fragment comprising a transcription factor and a DNA fragment in a body fluid sample obtained from a human or animal subject, which comprises the steps of:

(i) contacting the body fluid sample with a binding agent which binds to the transcription factor;

(ii) detecting or measuring the DNA fragment associated with the transcription factor; and

(iii) using the presence or amount of the DNA fragment as a measure of the amount of cell free chromatin fragments comprising the transcription factor in the sample.

2. The method according to claim 1, which comprises isolating the transcription factor bound in step (i) from the remaining body fluid sample, prior to detection of the associated DNA fragment in step (ii).

3 The method according to claim 1 or claim 2, wherein step (ii) comprises sequencing the DNA fragment associated with the transcription factor.

4. The method according to any one of claims 1 to 3, which additionally comprises extracting the DNA fragment associated with the transcription factor.

5. The method according to claim 4, which additionally comprises amplification of the extracted DNA fragment, such as by PCR.

6. The method according to any one of claims 1 to 5, wherein the DNA fragment associated with the transcription factor is detected and/or measured by real-time PCR, quantitative PCR, reverse transcriptase PCR, nested PCR, digital PCR, multiplex PCR, arbitrary primed PCR, cold PCR (co-amplification at lower denaturation temperature-PCR).

7. The method according to any one of claims 1 to 6, which additionally comprises removing cell free nucleosomes from the body fluid sample.

~~8. The method according to claim 7, which comprises contacting the body fluid sample with a binding agent which binds to nucleosomes or a component thereof and removing the sample bound to the binding agent prior to step (ii).~~

~~9. The method according to any one of claims 1 to 8, wherein the cell free chromatin fragment consists of the transcription factor and DNA fragment.~~

8~~10~~. The method according to any one of claims 1 to 7~~9~~, wherein the transcription factor bound by the binding agent in step (i) is washed with a buffer solution containing at least 1% concentration of detergent, prior to detection of the associated DNA fragment in step (ii).

9~~11~~. A method of detecting a disease in a human or animal subject which comprises the steps of:

(i) contacting a body fluid sample obtained from the human or animal subject with a binding agent which binds to a transcription factor;

(ii) detecting or measuring the DNA associated with the transcription factor; and

(iii) using the presence or amount of DNA as an indicator of the presence of a disease in the subject.

10~~2~~. The method according to claim ~~11~~9, which comprises using the transcription factor and sequence of the associated DNA as a combined biomarker for indicating the presence of the disease in the subject.

11~~3~~. A method of detecting a tissue affected by a disease in a human or animal subject which comprises the steps of:

(i) contacting a body fluid sample obtained from the human or animal subject with a binding agent which binds to a transcription factor;

(ii) sequencing the DNA associated with the transcription factor; and

(iii) using the presence of the transcription factor and the sequence of the associated DNA as a combined biomarker for determining the tissue affected by the disease in the subject.

12~~4~~. The method according to claim 11~~3~~, wherein the tissue affected by the disease is the organ of origin.

13~~5~~. The method according to any one of claims 11 to 12~~4~~, wherein the disease is cancer or an inflammatory disease.

14. The method according to any one of claims 1 to 13, wherein the transcription factor is CTCF.

156. The method according to any one of claims 1 to 145, wherein the binding agent which binds to the transcription factor is an antibody or a fragment thereof.

167. The method according to any one of claims 1 to 156, wherein the body fluid sample is a blood, serum or plasma sample.

178. The method according to any one of claims 1 to 167, wherein the body fluid sample is a plasma sample which obtained by: (1) contacting a whole blood sample with a cross-linking agent; (2) contacting the cross-linked sample with a calcium ion chelating agent; and (3) isolating plasma from the sample.

18. The method according to claim 17, wherein the cross-linking agent is formaldehyde or a formaldehyde releasing agent, and/or wherein the calcium ion chelating agent is EDTA.

~~19. A method for the assessment of an animal or a human subject for suitability for a medical treatment which comprises the steps of:~~

~~(i) detecting, measuring or sequencing DNA associated with a cell free chromatin fragment comprising a transcription factor in a body fluid sample obtained from the subject; and~~

~~(ii) using the associated DNA level and/or sequence detected in step (i) as a parameter for the selection of a suitable treatment for the subject.~~

~~20. A method for monitoring a treatment of an animal or a human subject which comprises the steps of:~~

~~(i) detecting, measuring or sequencing DNA associated with a cell free chromatin fragment comprising a transcription factor in a body fluid sample obtained from the subject;~~

~~(ii) repeating the detection, measurement or sequencing of DNA associated with a cell free chromatin fragment comprising the transcription factor in a body fluid sample obtained from the subject on one or more occasions; and~~

~~(iii) using any changes in the associated DNA level and/or DNA sequence detected in step (i) compared to step (ii) as a parameter for any changes in the condition of the subject.~~

~~21. The method according to claim 20, wherein the treatment is for the treatment of cancer.~~

~~22~~19. The method according to any one of claims 1 to ~~2~~18, wherein the DNA associated with a cell free chromatin fragment comprising the transcription factor is detected or measured as one of a panel of measurements.

20~~3~~. A kit for the detection of a cell free chromatin fragment comprising a transcription factor and a DNA fragment as a combination biomarker which comprises a ligand or binder for the transcription factor optionally together with reagents for the amplification and/or sequencing of DNA associated with said transcription factor, and/or a ligand or binder for nucleosomes and/or instructions for use of the kit in accordance with the method according to any one of claims 1 to ~~22~~19.

~~24. A method of treating cancer in a subject in need thereof, wherein said method comprises the following steps:~~
~~(a) contacting a body fluid sample obtained from the human or animal subject with a binding agent which binds to a transcription factor;~~
~~(b) detecting, measuring or sequencing a DNA fragment associated with the transcription factor; and~~
~~(c) using the presence, amount or sequence of DNA fragment as an indicator of the presence of cancer in the subject; and~~
~~(d) administering a treatment if the subject is determined to have cancer in step (c).~~

~~25. The method according to claim 24, wherein the treatment is selected from: surgery, radiotherapy, chemotherapy, immunotherapy, hormone therapy and biological therapy.~~

~~26. A method of detecting a disease in a human or animal fetus which comprises the steps of:~~
~~(i) obtaining a body fluid sample from a pregnant human or animal subject;~~
~~(ii) contacting the body fluid sample with a binding agent which binds to a transcription factor;~~
~~(iii) detecting, measuring or sequencing the DNA associated with the transcription factor; and~~

~~(iv) using the presence, sequence or amount of DNA as an indicator of the presence of a disease in the fetus.~~