

CLAIMS

1. *In vitro* use of a tissue specific transcription factor-nucleosome adduct or transcription cofactor-nucleosome adduct as a biomarker in a biological fluid for the detection or diagnosis of a cancer in a subject.
2. The *in vitro* use as defined in claim 1, wherein the tissue specific transcription factor-nucleosome adduct or transcription cofactor-nucleosome adduct is used to identify the site of development of the cancer in the subject.
3. A method for detecting a cancer and/or determining the site of development of a cancer in a subject which comprises the steps of:
 - (i) contacting a biological fluid sample obtained from the subject with a first binding agent which binds to nucleosomes or a component thereof, or a tissue specific transcription factor or cofactor adducted to a nucleosome;
 - (ii) contacting the nucleosomes or sample with a second binding agent which binds to a tissue specific transcription factor or cofactor adducted to a nucleosome when the first binding agent binds to the nucleosome or a component thereof, or said second binding agent binds to a nucleosome or component thereof when the first binding agent binds to a tissue specific transcription factor or cofactor adducted to a nucleosome; and
 - (iii) detecting or quantifying the binding of said second binding agent to the adducted tissue specific transcription factor or cofactor, nucleosomes or a component thereof in the sample;
 wherein the presence or level of the tissue specific transcription factor or cofactor adducted to a nucleosome is used as an indicator of the site of development of said cancer.
4. The method as defined in claim 3, which comprises the steps of:
 - (i) contacting a biological fluid sample obtained from the subject with a first binding agent which binds to nucleosomes or a component thereof;
 - (ii) contacting the nucleosomes or sample with a second binding agent which binds to a tissue specific transcription factor or cofactor adducted to a nucleosome; and
 - (iii) detecting or quantifying the binding of said second binding agent to the adducted tissue specific transcription factor or cofactor in the sample.

5. The method as defined in claim 3, which comprises the steps of:

- (i) contacting a biological fluid sample obtained from the subject with a first binding agent which binds to a tissue specific transcription factor or cofactor;
- (ii) contacting the sample with a second binding agent which binds to nucleosomes or a component thereof; and
- (iii) detecting or quantifying the binding of said second binding agent to nucleosomes or a component thereof in the sample.

6. The *in vitro* use as defined in claim 1 or claim 2, or the method as defined in any one of claims 3 to 5, wherein the cancer is a primary cancer.

7. The *in vitro* use as defined in claim 1 or claim 2, or the method as defined in any one of claims 3 to 6, wherein the subject is a subject with metastatic cancer of unknown primary cancer.

8. The *in vitro* use as defined in claim 1 or claim 2, or the method as defined in any one of claims 3 to 7, wherein the subject has previously been diagnosed with cancer.

9. The *in vitro* use or method as defined in claim 8, wherein the subject was previously diagnosed with cancer using circulating tumour DNA (ctDNA) as a biomarker.

10. The method as defined in any one of claims 3 to 9, wherein the binding agent is an antibody, an antibody fragment or an aptamer.

11. The method as defined in any one of claims 3 to 10, wherein the binding agent which binds to nucleosomes or a component thereof, is directed to bind to a particular histone, histone modification, histone variant or isoform, or to DNA or a component thereof.

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

- (i) detecting or measuring a tissue specific transcription factor or cofactor adducted to a nucleosome in a biological fluid of the subject as defined in the method of any one of claims 3 to 11; and

(ii) using the type of tissue specific transcription factor or cofactor adducted to a nucleosome detected to determine a suitable treatment for the subject.

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

(i) detecting or measuring a tissue specific transcription factor or cofactor adducted to a nucleosome in a biological fluid of the subject as defined in the method of any one of claims 3 to 11;

(ii) repeating the detection or measurement of the tissue specific
10 transcription factor or cofactor adducted to a nucleosome in a biological fluid of the subject on one or more occasions; and

(iii) using any changes in the level of tissue specific transcription factor or cofactor adducted to a nucleosome detected as a parameter for any changes in the condition of the subject.

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14. The *in vitro* use as defined in claim 1 or claim 2, or the method as defined in any one of claims 3 to 13 wherein the tissue specific transcription factor is selected from: GATA 3, CDX2, TTF-1, PAX8, WT1, NKX3.1, P63 or P40.

20 15. The *in vitro* use as defined in claim 1 or claim 2, or the method as defined in any one of claims 3 to 14, wherein the biological fluid is selected from: blood, serum or plasma.