

nucleic acid obtained from said non-cancerous biological sample; generating a matrix of sequencing tag counts for said at least one promoter based on said mapping; analysing said matrix of sequencing tag counts; and determining the differential enrichment of the at least one promoter in the nucleic acid relative to the at least one promoter in the reference nucleic acid using the analysis of said matrix of sequencing tag counts, wherein the differential enrichment of the at least one promoter in the cancerous biological sample obtained from the subject relative to that in the non-cancerous sample is indicative of the presence of a promoter associated with cancer in a subject.

[0010] In another aspect there is provided a method for determining the activity of at least one promoter in a cancerous biological sample relative to a non-cancerous biological sample, comprising: mapping isolated nucleic acid comprising at least one promoter sequence obtained from said cancerous biological sample against a reference nucleic acid obtained from said non-cancerous biological sample; generating a matrix of sequencing tag counts for said at least one promoter based on said mapping; analysing said matrix of sequencing tag counts; and determining the differential activity of the at least one promoter in the nucleic acid relative to the at least one promoter in the reference nucleic acid using the analysis of said matrix of sequencing tag counts.

[0010a] In another aspect, there is provided the use of a biomarker comprising at least one promoter having increased activity in a cancerous biological sample relative to a normal non-cancerous biological sample, wherein the promoter comprises an increase of SUZ12 binding sites relative to the total promoter population in the manufacture of a medicament for detecting cancer in a subject.

DEFINITIONS

[0011] The term “antigen binding protein” as used herein refers to antibodies, antibody fragments and other protein constructs, such as domains, which are capable of binding to an antigen.

[0012] The term “antibody” is used herein in the broadest sense to refer to molecules with an immunoglobulin-like domain and includes monoclonal, recombinant, polyclonal, chimeric, humanised, bispecific and heteroconjugate antibodies; a single variable domain, a domain antibody, antigen binding fragments, immunologically effective fragments, single chain Fv, diabodies, Tandabs™, etc (for a summary of alternative “antibody” formats see Holliger and Hudson, Nature Biotechnology, 2005, Vol 23, No. 9, 1126-1136).

[0013] The phrase “single variable domain” refers to an antigen binding protein variable domain (for example, V_H , V_{HH} , V_L) that specifically binds an antigen or epitope independently of a different variable region or domain.

mapping isolated nucleic acid comprising at least one promoter obtained from a cancerous biological sample of the subject against a reference nucleic acid obtained from a non-cancerous biological sample to obtain an RPKM or FPKM value for said at least one promoter; and

determining the differential activity of the at least one promoter in the nucleic acid relative to the activity of the at least one promoter in the reference nucleic acid using said RPKM or FPKM value, wherein an increased activity of the at least one promoter in the cancerous biological sample obtained from the subject relative to that in the non-cancerous sample is indicative of the presence of a promoter associated with cancer in a subject.

22. The method of claim 21, wherein the at least one promoter associated with cancer is present when an RKPM or FPKM value for the at least one promoter in the nucleic acid obtained from the biological sample is:

i) greater than between a 1 to 20-fold, such as a 1-fold, 2-fold, 3-fold, 4-fold or 5-fold, change in mean RPKM or FPKM value relative to the RPKM or FPKM value of the at least one promoter in the reference nucleic acid obtained from the non-cancerous biological sample; and

ii) greater than a 0.1 RPKM or FPKM range relative to the RPKM or FPKM value of the at least one promoter in the reference nucleic acid obtained from the non-cancerous biological sample.

~~A biomarker for detecting cancer in a subject, the~~ Use of a biomarker comprising at least one promoter having increased activity in a cancerous biological sample relative to a normal non-cancerous biological sample, wherein the promoter comprises an increase of SUZ12 binding sites relative to the total promoter population in the manufacture of a medicament for detecting cancer in a subject.

~~The use biomarker~~ of claim 23, wherein the at least one promoter exhibits a low DNA methylation level relative to the total promoter population.

25. The ~~use biomarker~~ of any one of claim 23 or 24, wherein the at least one promoter is positioned adjacent to a gene associated with cell-type specification, embryonic development or transcription factors.

26. The ~~use biomarker~~ of claim 25, wherein the gene is NKX6-3, SALL4, HOXB9, MET, TNK2, KLK1, FAR2, HOXA11 or HOXA11-AS.

27. The ~~use biomarker~~ of any one of claims 23-26, wherein the at least one promoter comprises a cryptic promoter.

28. A method for determining the presence of at least one promoter associated with cancer in a cancerous biological sample relative to a non-cancerous biological sample, comprising;

mapping isolated nucleic acid comprising at least one promoter sequence obtained from said cancerous biological sample against a reference nucleic acid obtained from said non-cancerous biological sample;

generating a matrix of sequencing tag counts for said at least one promoter based on said mapping;

analysing said matrix of sequencing tag counts; and

determining the differential enrichment of the at least one promoter in the nucleic acid relative to the at least one promoter in the reference nucleic acid using the analysis of said matrix of sequencing tag counts, wherein the differential enrichment of the at least one promoter in the cancerous biological sample obtained from the subject relative to that in the non-cancerous sample is indicative of the presence of a promoter associated with cancer in a subject.

29. A method for determining the activity of at least one promoter in a cancerous biological sample relative to a non-cancerous biological sample, comprising;

mapping isolated nucleic acid comprising at least one promoter sequence obtained from said cancerous biological sample against a reference nucleic acid obtained from said non-cancerous biological sample;