

CLAIMS

WHAT IS CLAIMED IS:

1. A computer-implemented method for detecting a presence or an absence of a cancer in a subject, the method comprising:
 - (a) providing a set of sequence reads from cell-free deoxyribonucleic acid (DNA) extracted from said subject;
 - (b) using said set of sequence reads to generate a coverage pattern at binding sites of a transcription factor;
 - (c) processing said coverage pattern to provide a signal, wherein said signal characterizes binding site accessibility of said binding sites of said transcription factor;
 - (d) splitting said coverage pattern into a low-frequency signal and a high-frequency signal using a low-pass filter;
 - (e) determining an accessibility score for each of said binding sites of said transcription factor based at least in part on said high-frequency signal; and
 - (f) detecting said presence or absence of said cancer in said subject, based at least in part on a deviation of said accessibility score from a reference accessibility score.
2. The method of claim 1, wherein (b) comprises aligning said set of sequence reads to a reference sequence to provide an aligned sequence pattern, selecting regions of said aligned sequence pattern that correspond to said binding sites of said transcription factor, and normalizing said aligned sequence pattern in said regions.
3. The method of claim 1, wherein said low-pass filter comprises a Savitzky-Golay filter.
4. The method of claim 3, wherein said Savitzky-Golay filter comprises a third-order Savitzky-Golay filter.
5. The method of claim 1, further comprising obtaining said low-frequency signal using a first Savitzky-Golay filter with a first window size, and obtaining said high-frequency signal using a second Savitzky-Golay filter with a second window size, wherein said first window size is larger than said second window size.
6. The method of claim 1, further comprising performing a locally weighted smoothing on said high-frequency signal.
7. The method of claim 6, wherein said locally weighted smoothing comprises a locally estimated scatterplot smoothing (LOESS).
8. The method of any one of claims 1-7, wherein said accessibility score that deviates from said reference accessibility score by greater than ± 3 mean of a standard deviation, is indicative of said presence of said cancer in said subject.

9. The method of any one of claims 1-8, wherein said subject is a human.
10. The method of any one of claims 1-9, wherein said transcription factor is an epithelial transcription factor.
11. The method of any one of claims 1-10, wherein said transcription factor is a cancer-specific transcription factor.
12. The method of claim 11, wherein said transcription factor is selected from the group consisting of FOXA1, GRHL1, GRHL2, and GRHL3.
13. The method of claim 11, wherein said transcription factor is selected from the group consisting of GRHL2, PU.1, LYL1, SPIB, AR, HOXB13, and NKX3-1.
14. The method of claim 11, wherein said transcription factor is selected from the group consisting of GRH-L2, ASH-2, HOX-B13, EVX2, PU.1, Lyl-1, Spi-B, FOXA1, HNF-1A, HNF-4A, HNF-4G, and DLX-2.
15. The method of claim 11, wherein said transcription factor is selected from the group consisting of GRHL2, FOXA1, and ZNF121; and wherein said cancer comprises breast cancer.
16. The method of claim 11, wherein said transcription factor is selected from the group consisting of EVX2, DLX2, HNF1A, HNF4A, GRHL2, and HNF4G; and wherein said cancer comprises colon cancer.
17. The method of claim 11, wherein said transcription factor is selected from the group consisting of LYL1 and PU.1, and wherein said cancer comprises colon cancer.
18. The method of claim 11, wherein said transcription factor is selected from the group consisting of GRHL2, FOXA1, HOXB13, AR, and NKX3-1; and wherein said cancer comprises prostate adenocarcinoma.
19. The method of claim 11, wherein said transcription factor is selected from the group consisting of REST, GRHL2, FOXA1, HOXB13, AR, and NKX3-1; and wherein said cancer comprises prostate small-cell neuroendocrine prostate cancer.
20. The method of claim 11, wherein said transcription factor is selected from the group consisting of GLIS1, SOX2, and SOX11; and wherein said cancer comprises prostate cancer.
21. The method of any one of claims 1-20, wherein (f) comprises identifying an increased accessibility score of a binding site of said transcription factor as compared to said reference accessibility score.
22. The method of claim 1, further comprising detecting said presence or absence of said cancer in said subject with an accuracy of at least about 70%.
23. The method of claim 1, further comprising detecting said presence or absence of said cancer in said subject with an accuracy of at least about 80%.
24. The method of claim 1, further comprising detecting said presence or absence of said cancer in said subject with an accuracy of at least about 90%.

25. The method of claim 1, further comprising detecting said presence of said cancer in said subject with a sensitivity of at least about 70%.
26. The method of claim 1, further comprising detecting said presence of said cancer in said subject with a sensitivity of at least about 80%.
27. The method of claim 1, further comprising detecting said presence of said cancer in said subject with a sensitivity of at least about 90%.
28. The method of claim 1, further comprising detecting said absence of said cancer in said subject with a specificity of at least about 70%.
29. The method of claim 1, further comprising detecting said absence of said cancer in said subject with a specificity of at least about 80%.
30. The method of claim 1, further comprising detecting said absence of said cancer in said subject with a specificity of at least about 90%.
31. The method of claim 1, further comprising detecting said presence of said cancer in said subject with a positive predictive value (PPV) of at least about 70%.
32. The method of claim 1, further comprising detecting said presence of said cancer in said subject with a positive predictive value (PPV) of at least about 80%.
33. The method of claim 1, further comprising detecting said presence of said cancer in said subject with a positive predictive value (PPV) of at least about 90%.
34. The method of claim 1, further comprising detecting said absence of said cancer in said subject with a negative predictive value (NPV) of at least about 70%.
35. The method of claim 1, further comprising detecting said absence of said cancer in said subject with a negative predictive value (NPV) of at least about 80%.
36. The method of claim 1, further comprising detecting said absence of said cancer in said subject with a negative predictive value (NPV) of at least about 90%.
37. The method of claim 1, further comprising detecting said presence or absence of said cancer in said subject with an Area Under the Receiver Operator Characteristic (AUROC) of at least about 0.70.
38. The method of claim 1, further comprising detecting said presence or absence of said cancer in said subject with an Area Under the Receiver Operator Characteristic (AUROC) of at least about 0.80.
39. The method of claim 1, further comprising detecting said presence or absence of said cancer in said subject with an Area Under the Receiver Operator Characteristic (AUROC) of at least about 0.90.
40. A system comprising a computing device comprising at least one computer processor, an operating system configured to perform executable instructions, a memory, and a computer

program including instructions executable by the computing device to provide a computer application for detecting a presence or an absence of a cancer in a subject, the computer application comprising:

- a sequence module programmed to obtain a set of sequence reads from cell-free deoxyribonucleic acid (DNA) extracted from said subject;
- a coverage module programmed to use said set of sequence reads to generate a coverage pattern at binding sites of a transcription factor;
- a signal module programmed to process said coverage pattern to provide a signal, wherein said signal characterizes binding site accessibility of said binding sites of said transcription factor;
- a splitting module programmed to split said coverage pattern into a low-frequency-signal and a high-frequency signal using a low-pass filter;
- a determination module programmed to determine an accessibility score for each of said binding sites of said transcription factor based at least in part on said high-frequency signal; and
- a detection module programmed to detect said presence or absence of said cancer in said subject, based at least in part on a deviation of said accessibility score from a reference accessibility score.

41. A non-transitory computer-readable medium comprising machine-executable code that, upon execution by one or more computer processors, implements a method for detecting a presence or an absence of a cancer in a subject, the method comprising:

- (a) providing a set of sequence reads from cell-free deoxyribonucleic acid (DNA) extracted from said subject;
- (b) using said set of sequence reads to generate a coverage pattern at binding sites of a transcription factor;
- (c) processing said coverage pattern to provide a signal, wherein said signal characterizes binding site accessibility of said binding sites of said transcription factor;
- (d) splitting said coverage pattern into a low-frequency signal and a high-frequency signal using a low-pass filter;
- (e) determining an accessibility score for each of said binding sites of said transcription factor based at least in part on said high-frequency signal; and
- (f) detecting said presence or absence of said cancer in said subject, based at least in part on a deviation of said accessibility score from a reference accessibility score.

42. A system for detecting a presence or an absence of a cancer in a subject, the system comprising:

- a database comprising a set of sequence reads from cell-free deoxyribonucleic acid (DNA) extracted from said subject; and

one or more computer processors operatively coupled to said database, wherein said one or more computer processors are individually or collectively programmed to:

- (a) use said set of sequence reads to generate a coverage pattern at binding sites of a transcription factor;
- (b) process said coverage pattern to provide a signal, wherein said signal characterizes binding site accessibility of said binding sites of said transcription factor;
- (c) split said coverage pattern into a low-frequency signal and a high-frequency signal using a low-pass filter;
- (d) determine an accessibility score for each of said binding sites of said transcription factor based at least in part on said high-frequency signal; and
- (e) detect said presence or absence of said cancer in said subject, based at least in part on a deviation of said accessibility score from a reference accessibility score.

43. A computer-implemented method for monitoring a progression or regression of a cancer in a subject, the method comprising:

- (a) providing a first set of sequence reads from cell-free deoxyribonucleic acid (DNA) extracted from said subject at a first time and a second set of sequence reads from cell-free DNA extracted from said subject at a second time that is later than said first time;
- (b) using said first set of sequence reads to generate a first coverage pattern at binding sites of a transcription factor and using said second set of sequence reads to generate a second coverage pattern at binding sites of said transcription factor;
- (c) processing said first coverage pattern to provide a first signal, wherein said first signal characterizes binding site accessibility of said binding sites of said transcription factor and processing said second coverage pattern to provide a second signal, wherein said second signal characterizes binding site accessibility of said binding sites of said transcription factor;
- (d) splitting said first coverage pattern into a first low-frequency signal and a first high-frequency signal using a first low-pass filter and splitting said second coverage pattern into a second low-frequency signal and a second high-frequency signal using a second low-pass filter;
- (e) determining a first accessibility score for each of said binding sites of said transcription factor based at least in part on said first high-frequency signal, and determining a second accessibility score for each of said binding sites of said transcription factor based at least in part on said second high-frequency signal; and
- (f) monitoring said progression or regression of said cancer in said subject, based at least in part on a deviation of said first accessibility score and said second

accessibility score from a reference accessibility score.

44. The method of claim 43, wherein (b) comprises aligning said first set of sequence reads and said second set of sequence reads to a reference sequence to provide a first aligned sequence pattern and a second aligned sequence pattern, respectively, selecting regions of said first aligned sequence pattern and said second aligned sequence pattern that correspond to binding sites of said transcription factor, and normalizing said first aligned sequence pattern and second aligned sequence pattern in said regions.

45. The method of claim 43, wherein said first and second low-pass filters comprise a Savitzky-Golay filter.

46. The method of claim 45, wherein said Savitzky-Golay filter comprises a third-order Savitzky-Golay filter.

47. The method of claim 45, further comprising obtaining said first and second low-frequency signals using a first Savitzky-Golay filter with a first window size, and obtaining said first and second high-frequency signals using a second Savitzky-Golay filter with a second window size, wherein said first window size is larger than said second window size.

48. The method of claim 43, further comprising performing a locally weighted smoothing on said first and second high-frequency signals.

49. The method of claim 48, wherein said locally weighted smoothing comprises a locally estimated scatterplot smoothing (LOESS).

50. The method of any one of claims 43-49, wherein said first and second accessibility scores that deviate from said reference accessibility score by greater than ± 3 mean of a standard deviation, is indicative of said presence of said cancer in said subject.

51. The method of any one of claims 43-50, wherein said subject is a human.

52. The method of any one of claims 43-51, wherein said transcription factor is a cancer-specific transcription factor.

53. The method of claim 52, wherein said transcription factor is selected from the group consisting of FOXA1, GRHL1, GRHL2, and GRHL3.

54. The method of claim 52, wherein said transcription factor is selected from the group consisting of GRHL2, PU.1, LYL1, SPIB, AR, HOXB13, and NKX3-1.

55. The method of claim 52, wherein said transcription factor is selected from the group consisting of GRH-L2, ASH-2, HOX-B13, EVX2, PU.1, Lyl-1, Spi-B, FOXA1, HNF-1a, HNF-4a, HNF-4g, and DLX-2.

56. The method of claim 52, wherein said transcription factor is selected from the group consisting of GRHL2, FOXA1, and ZNF121; and wherein said cancer comprises breast cancer.

57. The method of claim 52, wherein said transcription factor is selected from the group

consisting of EVX2, DLX2, HNF1A, HNF4A, GRHL2, and HNF4G; and wherein said cancer comprises colon cancer.

58. The method of claim 52, wherein said transcription factor is selected from the group consisting of LYL1 and PU.1, and wherein said cancer comprises colon cancer.

59. The method of claim 52, wherein said transcription factor is selected from the group consisting of GRHL2, FOXA1, HOXB13, AR, and NKX3-1; and wherein said cancer comprises prostate adenocarcinoma.

60. The method of claim 52, wherein said transcription factor is selected from the group consisting of REST, GRHL2, FOXA1, HOXB13, AR, and NKX3-1; and wherein said cancer comprises prostate small-cell neuroendocrine prostate cancer.

61. The method of claim 52, wherein said transcription factor is selected from the group consisting of GLIS1, SOX2, and SOX11; and wherein said cancer comprises prostate cancer.

62. The method of any one of claims 43-61, further comprising, based on (f), adjusting a therapeutic regimen for said cancer in said subject.

63. A system comprising a computing device comprising at least one computer processor, an operating system configured to perform executable instructions, a memory, and a computer program including instructions executable by the computing device to provide a computer application for monitoring a progression or regression of a cancer in a subject, the computer application comprising:

- a sequence module programmed to obtain a first set of sequence reads from cell-free deoxyribonucleic acid (DNA) extracted from said subject at a first time and a second set of sequence reads from cell-free DNA extracted from said subject at a second time that is later than said first time;

- a coverage module programmed to use said first set of sequence reads to generate a first coverage pattern at binding sites of a transcription factor and use said second set of sequence reads to generate a second coverage pattern at binding sites of said transcription factor;

- a signal module programmed to process said first coverage pattern to provide a first signal, wherein said first signal characterizes binding site accessibility of said binding sites of said transcription factor, and to process said second coverage pattern to provide a second signal, wherein said second signal characterizes binding site accessibility of said binding sites of said transcription factor;

- a splitting module programmed to split said first coverage pattern into a first low-frequency signal and a first high-frequency signal using a first low-pass filter and split said second coverage pattern into a second low-frequency signal and a second high-frequency signal using a second low-pass filter;

a determination module programmed to determine a first accessibility score for each of said binding sites of said transcription factor based at least in part on said first high-frequency signal and to determine a second accessibility score for each of said binding sites of said transcription factor based at least in part on said second high-frequency signal; and

a monitoring module programmed to monitor said progression or regression of said cancer in said subject, based at least in part on a deviation of said first accessibility score and said second accessibility score from a reference accessibility score.

64. A non-transitory computer-readable medium comprising machine-executable code that, upon execution by one or more computer processors, implements a method for monitoring a progression or regression of a cancer in a subject, the method comprising:

- (a) providing a first set of sequence reads from cell-free deoxyribonucleic acid (DNA) extracted from said subject at a first time and a second set of sequence reads from cell-free DNA extracted from said subject at a second time that is later than said first time;
- (b) using said first set of sequence reads to generate a first coverage pattern at binding sites of a transcription factor and using said second set of sequence reads to generate a second coverage pattern at binding sites of said transcription factor;
- (c) processing said first coverage pattern to provide a first signal, wherein said first signal characterizes binding site accessibility of said binding sites of said transcription factor and processing said second coverage pattern to provide a second signal, wherein said second signal characterizes binding site accessibility of said binding sites of said transcription factor;
- (d) splitting said first coverage pattern into a first low-frequency signal and a first high-frequency signal using a first low-pass filter and splitting said second coverage pattern into a second low-frequency signal and a second high-frequency signal using a second low-pass filter;
- (e) determining a first accessibility score for each of said binding sites of said transcription factor based at least in part on said first high-frequency signal, and determining a second accessibility score for each of said binding sites of said transcription factor based at least in part on said second high-frequency signal; and
- (f) monitoring said progression or regression of said cancer in said subject, based at least in part on a deviation of said first accessibility score and said second accessibility score from a reference accessibility score.

65. A system for monitoring a progression or regression of a cancer in a subject, the system comprising:

a database comprising a first set of sequence reads from cell-free deoxyribonucleic acid

(DNA) extracted from said subject at a first time and a second set of sequence reads from cell-free DNA extracted from said subject at a second time that is later than said first time; and

one or more computer processors operatively coupled to said database, wherein said one or more computer processors are individually or collectively programmed to:

(a) use said first set of sequence reads to generate a first coverage pattern at binding sites of a transcription factor and use said second set of sequence reads to generate a second coverage pattern at binding sites of said transcription factor;

(b) process said first coverage pattern to provide a first signal, wherein said first signal characterizes binding site accessibility of said binding sites of said transcription factor;

(c) split said first coverage pattern into a first low-frequency signal and a first high-frequency signal using a first low-pass filter;

(d) determine a first accessibility score for each of said binding sites of said transcription factor based at least in part on said first high-frequency signal;

(e) process said second coverage pattern to provide a second signal, wherein said second signal characterizes binding site accessibility of said binding sites of said transcription factor;

(f) split said second coverage pattern into a second low-frequency signal and a second high-frequency signal using a second low-pass filter;

(g) determine a second accessibility score for each of said binding sites of said transcription factor based at least in part on said second high-frequency signal; and

(h) monitor said progression or regression of said cancer in said subject, based at least in part on a deviation of said first accessibility score and said second accessibility score from a reference accessibility score.

66. A computer-implemented method, comprising:

(a) providing a first set of sequence reads from cell-free deoxyribonucleic acid (DNA) extracted from said subject at a first time and a second set of sequence reads extracted from cell-free DNA from said subject at a second time that is later than said first time;

(b) using said first set of sequence reads to generate a first coverage pattern at binding sites of a transcription factor and using said second set of sequence reads to generate a second coverage pattern at binding sites of said transcription factor;

(c) processing said first coverage pattern to provide a first signal, wherein said first signal characterizes binding site accessibility of said binding sites of said transcription factor;

(d) splitting said first coverage pattern into a first low-frequency signal and a first

high-frequency signal using a first low-pass filter;

- (e) determining a first accessibility score for each of said binding sites of said transcription factor based at least in part on said first high-frequency signal;
- (f) processing said second coverage pattern to provide a second signal, wherein said second signal characterizes binding site accessibility of said binding sites of said transcription factor;
- (g) splitting said second coverage pattern into a second low-frequency signal and a second high-frequency signal using a second low-pass filter;
- (h) determining a second accessibility score for each of said binding sites of said transcription factor based at least in part on said second high-frequency signal; and
- (i) determining a tumor-specific transcription factor binding site (TFBS) pattern, based at least in part on a deviation of said first accessibility score and said second accessibility score from a reference accessibility score.

67. A system comprising a computing device comprising at least one computer processor, an operating system configured to perform executable instructions, a memory, and a computer program including instructions executable by the computing device to provide a computer application for determining a tumor-specific transcription factor binding site (TFBS) pattern, the computer application comprising:

a sequence module programmed to obtain a first set of sequence reads from cell-free deoxyribonucleic acid (DNA) extracted from said subject at a first time and a second set of sequence reads extracted from cell-free DNA from said subject at a second time that is later than said first time;

a coverage module programmed to use said first set of sequence reads to generate a first coverage pattern at binding sites of a transcription factor and use said second set of sequence reads to generate a second coverage pattern at binding sites of said transcription factor;

a signal module programmed to process said first coverage pattern to provide a first signal, wherein said first signal characterizes binding site accessibility of said binding sites of said transcription factor, and to process said second coverage pattern to provide a second signal, wherein said second signal characterizes binding site accessibility of said binding sites of said transcription factor;

a splitting module programmed to split said first coverage pattern into a first low-frequency signal and a first high-frequency signal using a first low-pass filter and split said second coverage pattern into a second low-frequency signal and a second high-frequency signal using a second low-pass filter;

a determination module programmed to determine a first accessibility score for each of

said binding sites of said transcription factor based at least in part on said first high-frequency signal and to determine a second accessibility score for each of said binding sites of said transcription factor based at least in part on said second high-frequency signal; and

a detection module programmed to determine said tumor-specific TFBS pattern, based at least in part on a deviation of said first accessibility score and said second accessibility score from a reference accessibility score.

68. A non-transitory computer-readable medium comprising machine-executable code that, upon execution by one or more computer processors, implements a method for determining a tumor-specific transcription factor binding site (TFBS) pattern, the method comprising:

- (a) providing a first set of sequence reads from cell-free deoxyribonucleic acid (DNA) extracted from said subject at a first time and a second set of sequence reads extracted from cell-free DNA from said subject at a second time that is later than said first time;
- (b) using said first set of sequence reads to generate a first coverage pattern at binding sites of a transcription factor and using said second set of sequence reads to generate a second coverage pattern at binding sites of said transcription factor;
- (c) processing said first coverage pattern to provide a first signal, wherein said first signal characterizes binding site accessibility of said binding sites of said transcription factor;
- (d) splitting said first coverage pattern into a first low-frequency signal and a first high-frequency signal using a first low-pass filter;
- (e) determining a first accessibility score for each of said binding sites of said transcription factor based at least in part on said first high-frequency signal;
- (f) processing said second coverage pattern to provide a second signal, wherein said second signal characterizes binding site accessibility of said binding sites of said transcription factor;
- (g) splitting said second coverage pattern into a second low-frequency signal and a second high-frequency signal using a second low-pass filter;
- (h) determining a second accessibility score for each of said binding sites of said transcription factor based at least in part on said second high-frequency signal; and
- (i) determining said tumor-specific TFBS pattern, based at least in part on a deviation of said first accessibility score and said second accessibility score from a reference accessibility score.

69. A system for determining a tumor-specific transcription factor binding site (TFBS) pattern, the system comprising:

a database comprising a first set of sequence reads from cell-free deoxyribonucleic acid (DNA) extracted from said subject at a first time and a second set of sequence reads extracted from cell-free DNA from said subject at a second time that is later than said first time; and

one or more computer processors operatively coupled to said database, wherein said one or more computer processors are individually or collectively programmed to:

(a) use said first set of sequence reads to generate a first coverage pattern at binding sites of a transcription factor and use said second set of sequence reads to generate a second coverage pattern at binding sites of said transcription factor;

(b) process said first coverage pattern to provide a first signal, wherein said first signal characterizes binding site accessibility of said binding sites of said transcription factor;

(c) split said first coverage pattern into a first low-frequency signal and a first high-frequency signal using a first low-pass filter;

(d) determine a first accessibility score for each of said binding sites of said transcription factor based at least in part on said first high-frequency signal, and

(e) process said second coverage pattern to provide a second signal, wherein said second signal characterizes binding site accessibility of said binding sites of said transcription factor;

(f) split said second coverage pattern into a second low-frequency signal and a second high-frequency signal using a second low-pass filter;

(g) determine a second accessibility score for each of said binding sites of said transcription factor based at least in part on said second high-frequency signal; and

(h) determine said tumor-specific TFBS pattern, based at least in part on a deviation of said first accessibility score and said second accessibility score from a reference accessibility score.

70. A system for detecting a presence or an absence of a cancer in a subject, comprising a processor configured to:

(i) use sequence reads from cell-free deoxyribonucleic acid (DNA) extracted from said subject to generate a coverage pattern at binding sites of a transcription factor;

(ii) process said coverage pattern to provide a signal, wherein said signal characterizes binding site accessibility of said binding sites of said transcription factor;

(iii) split said coverage pattern into a low-frequency signal and a high-frequency signal using a low-pass filter;

(iv) determine an accessibility score for each of said binding sites of said

- transcription factor based at least in part on said high-frequency signal; and
- (v) provide a diagnosis of said cancer in said subject, based at least in part on a deviation of said accessibility score from a reference accessibility score.
71. The system of claim 70, further comprising identifying an increased accessibility score of a binding site of said transcription factor as compared to said reference accessibility score.
72. A system for monitoring a progression or regression of a cancer in a subject, comprising a processor configured to:
- (i) use a first set of sequence reads from cell-free deoxyribonucleic acid (DNA) extracted from said subject at a first time and a second set of sequence reads from cell-free DNA extracted from said subject at a second time that is later than said first time to generate a first coverage pattern at binding sites of a transcription factor and a second coverage pattern at binding sites of said transcription factor;
 - (ii) process said first coverage pattern to provide a first signal, wherein said first signal characterizes binding site accessibility of said binding sites of said transcription factor and process said second coverage pattern to provide a second signal, wherein said second signal characterizes binding site accessibility of said binding sites of said transcription factor;
 - (iii) split said first coverage pattern into a first low-frequency signal and a first high-frequency signal using a first low-pass filter and split said second coverage pattern into a second low-frequency signal and a second high-frequency signal using a second low-pass filter;
 - (iv) determine a first accessibility score for each of said binding sites of said transcription factor based at least in part on said first high-frequency signal, and determining a second accessibility score for each of said binding sites of said transcription factor based at least in part on said second high-frequency signal; and
 - (v) monitor said progression or regression of said cancer in said subject, based at least in part on a deviation of said first accessibility score and said second accessibility score from a reference accessibility score.
73. The system of claim 72, wherein said transcription factor is selected from the group consisting of GRH-L2, ASH-2, HOX-B13, EVX2, PU.1, Lyl-1, Spi-B, FOXA1, HNF-1a, HNF-4a, HNF-4g, and DLX-2.