

What is claimed is:

1. A method of determining microsatellite instability (MSI) comprising:
 - (i) determining a tract-based score based on somatic allele lengths in a plurality of tracts of nucleotide repeats in sequenced DNA in a sample obtained from a subject;
 - (ii) determining the presence of somatic mutations in the DNA in regions outside of the plurality of tracts of nucleotide repeats;
 - (iii) determining a genomic signature score of the somatic mutations found outside of the plurality of tracts of nucleotide repeats based on genomic signatures of mismatch repair deficiency;
 - (iv) determining an MSI score for the sample based on the tract-based score and the genomic signature score; and
 - (v) classifying the sample as microsatellite instability-high (MSI-H) or microsatellite-stable (MSS) based on the MSI score.
2. The method of claim 1, further comprising preparing a report comprising the MSI score and a classification of the sample as microsatellite instability-high (MSI-H) or microsatellite-stable (MSS).
3. The method of claim 1, wherein the sample is a tumor sample.
4. The method of claim 1, wherein the plurality of tracts of nucleotide repeats comprises mononucleotide repeats, dinucleotide repeats, trinucleotide repeats, tetranucleotide repeats, pentanucleotide repeats, hexanucleotide repeats, heptanucleotide repeats, octanucleotide repeats, or combinations thereof.
5. The method of claim 4, wherein the plurality of tracts of nucleotide repeats comprises mononucleotide repeats.
6. The method of claim 1, wherein tracts of nucleotide repeats in MSI-H samples are shorter relative to tracts of nucleotide repeats in reference samples.
7. The method of claim 1, wherein tracts of nucleotide repeats in MSI-H samples are at least two base pairs shorter relative to tracts of nucleotide repeats in reference samples.
8. The method of claim 6, wherein the reference samples are matched normal samples or MSS samples.

9. The method of claim 6, further comprising determining a frequency of shorter tracts of nucleotide repeats.
10. The method of claim 1, wherein the plurality of tracts of nucleotide repeats comprises one or more microsatellite markers.
11. The method of claim 10, wherein the one or more microsatellite markers are selected from human genome microsatellite markers.
12. The method of claim 1, wherein genomic signatures of the somatic mutations comprise eleven base pairs surrounding the somatic mutations.
13. The method of claim 1, wherein somatic mutations are classified as associated with an MSI-H sample or an MSS sample based on the genomic signature score.
14. The method of claim 1, wherein a treatment to the subject is to be selected or administered based on the MSI score.
15. The method of claim 14, wherein the MSI score indicates that the sample of the subject is microsatellite instability-high (MSI-H) and the treatment comprises an immune checkpoint inhibitor.
16. The method of claim 15, wherein the immune checkpoint inhibitor comprises an antibody.
17. The method of claim 16, wherein the antibody is selected from the group consisting of: an anti-PD-1 antibody; an anti-IDO antibody; an anti-CTLA-4 antibody; an anti-PD-L1 antibody; and an anti-LAG-3 antibody.
18. The method of claim 16, wherein the checkpoint inhibitor is Pembrolizumab, Nivolumab, Atezolizumab, or Ipilimumab.
19. The method of claim 1, wherein sequenced DNA in the sample comprises one or more sequenced genomes, one or more sequenced exomes, or regions of one or more sequenced genomes or one or more sequenced exomes.