CLAIMS

What is claimed is:

1. A method of predicting therapeutic outcome for immune therapy of a cancer, comprising:
   obtaining omics data from a tumor of a patient;
   identifying at least one of an APOBEC mutational signature and a POLE mutational signature in the omics data;
   quantifying expression of a plurality of genes associated with checkpoint inhibition from the omics data;
   determining an MSI status from the omics data; and
   using the APOBEC mutational signature and/or POLE mutational signature, the determined expression quantity of the plurality of genes, and the MSI status to update or generate a patient profile that indicates a prediction of therapeutic outcome for the immune therapy of the cancer.

2. The method of claim 1 further comprising a step of identifying at least one additional mutational signature.

3. The method of claim 2 wherein the additional mutational signature is a kataegis signature, an Ig gene hypermutation signature, a smoking mutational signature, an age related mutational signature, a UV light mutational signature, or a DNA MMR related mutational signature.

4. The method of any of the preceding claims wherein the immune therapy comprises at least two of a vaccine component, a cell-based component, and a checkpoint inhibition component.

5. The method of any of the preceding claims wherein the omics data comprise at least one of whole genome sequencing data, RNA sequencing data, transcription level data, cfDNA sequence data, cfRNA sequence data, and proteomics data.

6. The method of any of the preceding claims wherein the omics data comprise at least two of whole genome sequencing data, RNA sequencing data, transcription level data, cfDNA sequence data, cfRNA sequence data, and proteomics data.

7. The method of any of the preceding claims wherein the omics data are normalized against omics data from a healthy tissue of the same patient.

8. The method of any of the preceding claims wherein the APOBEC signature is selected from the group consisting of TpCpS→TpKpS, TpCpN→TpApN, and TpCpW→TpKpW, wherein S is C or G, K is G or T, N is C or G or A or T, and W is A or T.

9. The method of any of the preceding claims wherein the POLE signature is selected from the group consisting of TpCpT→TpApT and TpTpT→TpGpT.

10. The method of any of the preceding claims wherein the genes associated with checkpoint inhibition are selected from the group consisting of IDO, TDO, TIM3, CD40, LAG3, PD-L1, PD-L2, CTLA4, PD1, and IL2.

11. The method of claim 10 wherein the plurality of genes are at least five genes.

12. The method of any of the preceding claims wherein the MSI status is inferred from a quantity of neoepitopes that bind to an MHC complex of the patient.

13. The method of any of the preceding claims wherein the prediction of therapeutic outcome for the immune therapy of the cancer is a qualitative prediction.

14. The method of claim 13 wherein presence of the APOBEC mutational signature and/or the POLE mutational signature is indicative of a favorable therapeutic outcome.

15. The method of claim 13 wherein a positive MSI is indicative of a favorable therapeutic outcome.

16. The method of claim 13 wherein over-expression of the plurality of genes associated with checkpoint inhibition is indicative of a favorable therapeutic outcome.

17. The method of any of the preceding claims further comprising a step of determining pathway activity for Th1 T cell activation, cytotoxic T cell activation, and natural killer cell activation.