

WHAT IS CLAIMED IS:

1. A method of quantifying a diversity of at least one HLA allele pair in a subject, the method comprising:

obtaining DNA sequences of one or more HLA allele pairs in the subject;

comparing the DNA sequences of the one or more HLA allele pairs ~~to obtain alignment scores to~~ the sequences of all HLA allele pairs in a population of subjects by performing a pairwise alignment of the DNA sequences of the one or more HLA allele pairs with the sequences of all HLA allele pairs in the population to obtain alignment scores for the one or more HLA allele pairs;

obtaining a distribution of the alignment scores for the one or more HLA allele pairs; ~~and~~

determining a percentile score for the at least one HLA allele pair relative to the distribution of the alignment scores ~~for all HLA allele pairs; and~~

calculating a diversity score of the at least one HLA allele pair.

2. The method of claim 1, further comprising comparing the percentile score to a first predetermined threshold.

3. The method of claim 1, wherein the at least one HLA allele pair comprises any pair of HLA A, B, C, E, F, G, H, J, K, L, DP, DQ, and DR alleles.

4. The method of claim ~~1~~2, wherein if the percentile score is equal to or greater than the first predetermined threshold, the subject is recommended a first treatment.

5. The method of claim ~~1~~4, wherein if the percentile score is less than the first predetermined threshold, the subject is recommended a second treatment.

6. The method of claim ~~1~~5, wherein the method further comprises:

determining an expression level of the one or more HLA allele pairs;

obtaining an expression level score of the at least one HLA allele pair relative to the expression levels of the one or more HLA allele pairs;

determining a weighted percentile score for the at least one HLA allele pair, based on the expression level score of the at least one HLA allele pair, relative to the distribution of the alignment scores for the one or more HLA allele pairs;

comparing the weighted percentile score to a second predetermined threshold.

7. The method of claim 6, wherein if the weighted percentile score is equal to or greater than the second predetermined threshold, the subject is recommended ~~a~~the first treatment.

8. The method of claim 6, wherein if the weighted percentile score is less than the second predetermined threshold, the subject is recommended ~~a~~the second treatment.

9. The method of claim 2, wherein the first predetermined threshold is about 75%.

10. The method of claim 6, wherein the second predetermined threshold is about 75%.

11. The method of claim 4, wherein the first treatment comprises an immune checkpoint inhibitor (ICI).

12. The method of claim 5, wherein the second treatment comprises a non-immune checkpoint inhibitor (ICI).

13. The method of claim 2, if first predetermined threshold is equal to or greater than 50%, then the subject is further recommended a first additional treatment.

14. The method of claim 6, if the second predetermined threshold is less than 50%, then the subject is further recommended a second additional treatment.

15. The method of claim 6, wherein the expression level is an expression level of RNA, an expression level of protein, or both.

16. The method of ~~any one of the preceding claims~~claim 4, wherein the quantifying is repeated over time to determine if there is a change in the percentile score relative to the first predetermined threshold.

17. The method of ~~any one of the preceding claims~~claim 6, wherein the quantifying is repeated over time to determine if there is a change in the percentile score relative to the second predetermined threshold.

18. The method of any one of the preceding claims, wherein the quantifying comprises an assessment of TCR clonality.

19. A method of determining the predicted efficacy of a cancer treatment in a patient, comprising:

calculating a hazard ratio of HLA allele pairs in the patient, wherein the hazard ratio reflects the allelic diversity of the HLA allele pairs in the patient

determined by obtaining diversity scores of the HLA allele pairs in the patient relative to all HLA allele pairs in a population of subjects;

comparing the hazard ratio to a predetermined threshold, wherein a hazard ratio above the predetermined threshold indicates that the patient is predicted to have a high efficacy for a cancer treatment, and a hazard ratio below the predetermined threshold indicates that the patient is predicted to have a low efficacy for a cancer treatment.

20. The method of claim 19, wherein the cancer is a tumor and further comprising measuring a tumor burden score for the patient and comparing the tumor burden score to a predetermined threshold as a factor in determining the efficacy of a cancer treatment.

21. The method of claim 1, wherein the method is performed for all subjects in the population.

22. The method of claim 21, further comprising categorizing the subjects based on the diversity score as either having an upper 20% diversity score in at least one loci and high tumor mutational burden (TMB) or having lower 80% diversity score in all loci and low TMB.