

CLAIMS

Now, therefore, the following is claimed:

1. A method for using immunorepertoire diversity to assess a normal or abnormal status of an individual patient's immunorepertoire, the method comprising the steps of:

(a) using primers directed to pCDR3 sequences, shared by and identified from a reference group of individuals, to detect the presence in the patient's immunorepertoire of individual CDR3s within that shared group of pCDR3 sequences; and

(b) identifying the percentage of pCDR3 sequences from that shared group that are found within the patient's immunorepertoire to assess the status of the patient's immunorepertoire, wherein the presence of a minimum percentage of shared pCDR3 sequences represents a normal immunorepertoire, and the absence of a minimum percentage of shared pCDR3 sequences represents an abnormal immunorepertoire, relative to such shared group.

2. The method of claim 1 wherein the population of cells is selected from the group consisting of all T cells [panT], CD8+ T cells [cytotoxic T (Ta)], CD4+ T cells and their subsets [TH1, TH2, TH17, regulatory T (Treg), follicular T (TFH)], developmental subsets of T cells, such as naive T (Tn), activated T (Ta), memory T (Tm), all B cells (panB), naive B (Br), activated B (Ba), memory B (Bm), plasma and plasmablast B cells.

3. The method of claim 1, wherein the minimum percentage of pCDR3 is a percentage number selected from about 25 percent to about 75 percent.

4. The method of claim 1, wherein the minimum percentage of pCDR3 is about 25 percent.

5. The method of claim 1, where the pCDR3 is composed of about the 1000 most-frequently-shared CDR3.

6. The method of claim 1, where the pCDR3 is composed of more than 1000 of the most-frequently-shared CDR3.

7. The method of claim 1, where the pCDR3 is composed of fewer than 1000 of the most-frequently-shared CDR3.
8. The method of claim 1, wherein the pCDR3 is composed of CDR3 shared by at least 25 percent of a pool of individuals.
9. The method of claim 1, wherein the pCDR3 is composed of CDR3 shared by at least 50 percent of a pool of individuals.
10. The method of claim 9, wherein the pool contains at least 100 individuals.
11. The method of claim 9, wherein the pool contains about 1000 individuals.
12. A method for determining the immunorepertoire diversity in a patient, the method comprising:
 - (a) amplifying polynucleotides from a population of white blood cells from a human or animal subject in a reaction mix comprising target-specific nested primers to produce a set of first amplicons, at least a portion of the target-specific nested primers comprising additional nucleotides which, during amplification, serve as a template for incorporating into the first amplicons a binding site for at least one common primer;
 - (b) transferring a portion of the first reaction mix containing the first amplicons to a second reaction mix comprising at least one common primer;
 - (c) amplifying, using the at least one common primer, the first amplicons to produce a set of second amplicons;
 - (d) sequencing the second amplicons to identify CDR3 sequences in the subpopulation of white blood cells;
 - (e) using the identified CDR3 sequences to quantify the percentage of pCDR3 represented by the sample to provide a normality index; and
 - (f) identifying whether the normality index is normal or abnormal, wherein a normal state is characterized by the presence of a minimum percentage of pCDR3 and an abnormal state is characterized by the absence of a minimum percentage of pCDR3.

13. The method of claim 12, wherein the population of cells is selected from the group consisting of all T cells [panT], CD8+ T cells [cytotoxic T (Ta)], CD4+ T cells and their subsets [TH1, TH2, TH17, regulatory T (Treg), follicular T (TFH)], developmental subsets of T cells, such as naive T (Tn), activated T (Ta), memory T (Tm), all B cells (panB), naive B (Br), activated B (Ba), memory B (Bm), plasma and plasmablast B cells.

14. The method of claim 12, wherein the population of white blood cells is about 100,000 randomly-selected cells.

15. The method of claim 12, wherein the method is repeated about 10 to 100 times, each time with a random selection of cells, to determine the average percentage of pCDR3 expressed by the patient.

16. The method of claim 12, wherein the minimum percentage of pCDR3 is a percentage number from about 25 to about 75.

17. The method of claim 12, wherein the minimum percentage of pCDR3 is about 25 percent.

18. The method of claim 12, wherein the pCDR3 is composed of at least the 1000 most-frequently-shared CDR3.

19. The method of claim 12, wherein the pCDR3 includes SEQ ID NO:1 through SEQ ID NO: 4014.

20. The method of claim 12, wherein the pCDR3 is composed of CDR3 shared by at least 50 percent of a pool of individuals.

21. The method of claim 20, wherein the pool contains at least 100 individuals.

22. The method of claim 20, wherein the pool contains about 1000 individuals.

23. The method of claim 20, wherein the pool is composed of healthy control individuals.

24. The method of claim 20, wherein the pool is composed of individuals with one or more specific disease states.

25. The method of claim 20, wherein the pool of individuals is approximately age-matched to the patient.

26. The method of claim 20, wherein the pool of individuals is gender-matched to the patient.