CLAIMS

WHAT IS CLAIMED IS:

1. A method for processing a biological sample of a subject, comprising:
   (a) generating a subset of nucleic acid molecules from said biological sample using a pool of nucleic acid probes, wherein said probes comprise (i) a first plurality of nucleic acid probes configured to target elements of a human genome and (ii) a second plurality of nucleic acid probes configured to target elements of one or more non-human genome(s); and
   (b) subjecting said subset of nucleic acid molecules to an assay to yield sequence information comprising sequences of (i) human nucleic acids from said biological sample from said subject and (ii) non-human nucleic acids from said biological sample of said subject.
2. The method of claim 1, wherein said first plurality of nucleic acid probes of (i) are configured to target elements derived from said human genome.
3. The method of claim 1, wherein said second plurality of nucleic acid probes are configured to target elements from non-human genome sequences of one or more species selected from the group consisting of viruses, bacteria, bacterial phages, fungi, protists, archea, amoeba, helminths, algae, genetically modified cells, and genetically modified vectors.
4. The method of claim 1, wherein generating said subset of nucleic acid molecules from said biological sample comprises conducting one or more hybridization reactions.
5. The method of claim 1, further comprising obtaining said biological sample from said subject, wherein said biological sample is derived from a tumor biopsy, whole blood, or blood plasma.
6. The method of claim 1, further comprising aligning said sequences of said subset of nucleic acid molecules to one or more reference sequences.
7. The method of claim 6, wherein said one or more references sequences comprise a plurality of reference sequences, and wherein said plurality of references sequences correspond to two or more different species.
8. The method of claim 6, further comprising identifying sources of said nucleic acid molecules in said subset based on said alignment.
9. The method of claim 8, further comprising generating an output comprising said sources of said nucleic acid molecules in said biological sample.

10. The method of claim 1, wherein a concentration of said second plurality of nucleic acid probes is greater than a concentration of said first plurality of nucleic acid probes in said pool of nucleic acid probes.

11. The method of claim 1, wherein a concentration of said second plurality of nucleic acid probes in said pool of probes is greater than a concentration of said first plurality of nucleic acid probes in said pool of nucleic acid probes.

12. The method of claim 1, wherein said first plurality of nucleic acid probes comprises a human exome capture probe set.

13. The method of claim 1, wherein said first plurality of nucleic acid probes comprises probes configured to target junction sequences created by human V(D)J rearrangement or recombination.

14. The method of claim 1, wherein said second plurality of nucleic acid probes comprises one or more probes configured to target: human papilloma virus E6 gene, E7 gene, and/or one or more elements of a bacterial 16S ribosomal RNA gene.

15. The method of claim 1, wherein said assay of (b) comprises performing sequencing to generate paired-end read sequences of lengths from 130 bases to 280 bases.

16. The method of claim 1, further comprising producing one or more biomedical reports comprising one or more sets of data selected from the group consisting of: (i) candidate tumor neoantigens, (ii) detected non-human species, (iii) detected complementarity-determining region 3 (CDR3) sequences, and any combination thereof.

17. The method of claim 16, wherein said detected non-human species are antigens, and wherein said CDR3 sequences are capable of binding an antigen.

18. The method of claim 16, wherein said one or more biomedical reports comprises any two of (i)-(iii).

19. A method for processing a biological sample of a subject, comprising:

(a) generating a subset of nucleic acid molecules from said biological sample, wherein said subset of nucleic acid molecules comprises (i) a first plurality of nucleic acid molecules from said subject and (ii) a second plurality of nucleic acid molecules that are not from said subject, and wherein an abundance of said first plurality of nucleic acid molecules is greater than an abundance of said second plurality of nucleic acid molecules in said biological sample; and

(b) subjecting said subset of nucleic acid molecules to an assay to yield sequence information comprising sequences of (i) said first plurality of nucleic acid molecules and (ii) said second plurality of nucleic acid molecules.

20. The method of claim 19, wherein said nucleic acid molecules of (i) are derived from a genome of said subject.

21. The method of claim 19, wherein said second plurality of nucleic acid molecules that are not from said subject comprise one or more members selected from the group consisting of viruses, bacteria, bacterial phages, fungi, protists, archaea, amoeba, helminths, algae, genetically modified cells, and genetically modified vectors.

22. The method of claim 19, wherein generating said subset of nucleic acid molecules from said biological sample comprises conducting one or more hybridization reactions.

23. The method of claim 19, further comprising obtaining said biological sample from said subject, wherein said biological sample is derived from a tumor biopsy, whole blood, or blood plasma.

24. The method of claim 19, further comprising aligning said sequences of said subset of nucleic acid molecules to one or more reference sequences.

25. The method of claim 24, wherein said one or more references sequences comprise a plurality of reference sequences and wherein said plurality of references sequences correspond to two more different species.

26. The method of claim 24, further comprising identifying sources of said nucleic acid molecules in the subset based on said alignment.

27. The method of claim 26, further comprising generating an output comprising said identified sources of nucleic acid molecules in said biological sample.

28. The method of claim 19, wherein an abundance of said first plurality of nucleic acid molecules is greater than an abundance of said first plurality of nucleic acid molecules in said biological sample.

29. The method of claim 19, wherein a relative abundance of said second plurality of nucleic acid molecules in said subset is greater than a relative abundance of said first plurality of nucleic acid molecules in said subset.

30. A system for processing a biological sample of a subject, comprising:

a processing unit comprising one or more computer processors that are individually or collectively programmed to subject a subset of nucleic acid molecules to an assay to yield sequence information comprising sequences of (i) human nucleic acids from said biological sample from said subject and (ii) non-human nucleic acids from said biological sample of said subject, which subset of nucleic acid molecules is generated from said biological sample using a pool of nucleic acid probes, wherein said probes comprise (i) a first plurality of nucleic acid probes configured to target elements of a

human genome and (ii) a second plurality of nucleic acid probes configured to target elements of one or more non-human genome(s); and

computer memory configured to store said sequence information.

31. The system of claim 30, wherein said one or more computer processors are programmed to generate an alignment of said sequences to one or more reference sequences.

32. The system of claim 31, wherein said one or more references sequences comprise a plurality of reference sequences, and wherein said plurality of references sequences correspond to two or more different species.

33. The system of claim 31, wherein said one or more computer processors are programmed to identify sources of said nucleic acid molecules in said subset based on said alignment.

34. The system of claim 33, wherein said one or more computer processors are programmed to generate an output comprising said sources of said nucleic acid molecules in said biological sample.

35. The system of claim 30, wherein said one or more computer processors are programmed to produce one or more biomedical reports comprising information selected from the group consisting of: (i) candidate tumor neoantigens, (ii) detected non-human species, (iii) detected complementarity-determining region 3 (CDR3) sequences, and any combination thereof.

36. A system for processing a biological sample of a subject, comprising:

a processing unit comprising one or more computer processors that are individually or collectively programmed to subject a subset of nucleic acid molecules to an assay to yield sequence information comprising sequences of (i) said first plurality of nucleic acid molecules and (ii) said second plurality of nucleic acid molecules, which subset of nucleic acid molecules is generated from said biological sample, wherein said subset of nucleic acid molecules comprises (i) a first plurality of nucleic acid molecules from said subject and (ii) a second plurality of nucleic acid molecules that are not from said subject, and wherein an abundance of said first plurality of nucleic acid molecules is greater than an abundance of said second plurality of nucleic acid molecules in said biological sample; and

computer memory configured to store said sequence information.

37. The system of claim 36, wherein said one or more computer processors are programmed to generate an alignment of said sequences to one or more reference sequences.

38. The system of claim 37, wherein said one or more references sequences comprise a plurality of reference sequences, and wherein said plurality of references sequences correspond to two or more different species.

39. The system of claim 37, wherein said one or more computer processors are programmed to identify sources of said nucleic acid molecules in said subset based on said alignment.

40. The system of claim 38, wherein said one or more computer processors are programmed to generate an output comprising said sources of said nucleic acid molecules in said biological sample.

41. The system of claim 36, wherein said one or more computer processors are programmed to produce one or more biomedical reports comprising information selected from the group consisting of: (i) candidate tumor neoantigens, (ii) detected non-human species, (iii) detected complementarity-determining region 3 (CDR3) sequences, and any combination thereof.

CLAIMS

WHAT IS CLAIMED IS:

1. A method for processing a biological sample of a human subject, comprising:

(a) providing said biological sample from said human subject, wherein said biological sample of said human subject comprises (i) human nucleic acid molecules derived from said human subject, and (ii) non-human nucleic acid molecules derived from one or more non-human species, wherein said biological sample is derived from a tumor biopsy, whole blood, or blood plasma, wherein an amount of said human nucleic acid molecules derived from said human subject is 1,000 times or more greater than said non-human nucleic acid molecules derived from a non-human species;

(b) enriching said human nucleic acid molecules and said non-human nucleic acid molecules derived from said biological sample using a set of nucleic acid capture probes attached to a hybridization array or one or more beads, to yield an enriched set of nucleic acid molecules comprising (i) a subset of said human nucleic acids derived from said human subject and (ii) a subset of said non-human nucleic acids derived from one or more non-human species, wherein said set of nucleic acid capture probes comprises (i) a first plurality of nucleic acid probes configured to target elements of a human genome and (ii) a second plurality of nucleic acid probes configured to target elements of one or more non-human genome(s), wherein said first plurality of nucleic acid probes comprises probes configured to target junction sequences created by human V(D)J rearrangement or recombination, wherein said second plurality of nucleic acid probes comprises one or more probes configured to target: human papilloma virus E6 gene, human papilloma virus E7 gene, or one or more elements of a bacterial 16S ribosomal RNA gene; and

(c) sequencing said enriched set of nucleic acid molecules to yield sequence information comprising sequences of said enriched set of nucleic acid molecules, where said sequences of said enriched set of nucleic acid molecules comprise sequences of (i) human nucleic acids from said biological sample from said human subject and (ii) non-human nucleic acids from said biological sample of said human subject.

2. The method of claim 1, wherein enriching said human nucleic acid molecules and said non-human nucleic acid molecules derived from said biological sample comprises conducting one or more hybridization reactions.

3. The method of claim 1, wherein a concentration of said second plurality of nucleic acid probes is greater than a concentration of said first plurality of nucleic acid probes in said set of nucleic acid capture probes.

4. The method of claim 1, wherein a concentration of said second plurality of nucleic acid probes in said set of nucleic acid capture probes is greater than a concentration of said first plurality of nucleic acid probes in said set of nucleic acid capture probes.

5. The method of claim 1, wherein said first plurality of nucleic acid probes comprises a human exome capture probe set.

6. The method of claim 1, wherein said sequencing comprises performing sequencing to generate paired-end read sequences of lengths from 130 bases to 280 bases.

7. The method of claim 1, wherein said enriching comprises differentially enriching said human nucleic acid molecules and said non-human nucleic acid molecules.

8. The method of claim 1, wherein said enriching comprises enriching said human nucleic acid molecules and said non-human nucleic acid molecules, concurrently.

9. The method of claim 1, wherein said enriching comprises enriching said human nucleic acid molecules and said non-human nucleic acid molecules in a same sample volume.

10. The method of claim 1, further comprising amplifying said enriched set of nucleic acid molecules of (b) prior to sequencing in (c) to yield said sequence information.

11. The method of claim 1, wherein said biological sample is derived from said tumor biopsy.

12. The method of claim 1, wherein said biological sample is derived from said whole blood.

13. The method of claim 1, wherein said biological sample is derived from said blood plasma.

14. The method of claim 1, wherein said second plurality of nucleic acid probes comprises one or more probes configured to target said human papilloma virus E6 gene.

15. The method of claim 1, wherein said second plurality of nucleic acid probes comprises one or more probes configured to target said human papilloma virus E7 gene.

16. The method of claim 1, wherein said second plurality of nucleic acid probes comprises one or more probes configured to target said one or more elements of said bacterial 16S ribosomal RNA gene.

17. The method of claim 1, wherein said second plurality of nucleic acid probes comprises one or more probes configured to target said human papilloma virus E6 gene and said human papilloma virus E7 gene.

18. The method of claim 1, wherein said second plurality of nucleic acid probes comprises one or more probes configured to target said human papilloma virus E6 gene, said human papilloma virus E7 gene and said one or more elements of said bacterial 16S ribosomal RNA gene.

19. The method of claim 1, wherein enriching of (b) is performed using said set of nucleic acid capture probes attached to said hybridization array.

20. The method of claim 1, wherein enriching of (b) is performed using said one or more beads.

21. The method of claim 11, and wherein said second plurality of nucleic acid probes comprises one or more probes configured to target said human papilloma virus E6 gene or said human papilloma virus E7 gene.

22. The method of claim 11, wherein said second plurality of nucleic acid probes comprises one or more probes configured to target said one or more elements of said bacterial 16S ribosomal RNA gene.

23. The method of claim 12, wherein said second plurality of nucleic acid probes comprises one or more probes configured to target said human papilloma virus E6 gene or said human papilloma virus E7 gene.

24. The method of claim 12, wherein said second plurality of nucleic acid probes comprises one or more probes configured to target said one or more elements of said bacterial 16S ribosomal RNA gene.

25. The method of claim 13, wherein said second plurality of nucleic acid probes comprises one or more probes configured to target said human papilloma virus E6 gene or said human papilloma virus E7 gene.

26. The method of claim 13, wherein said second plurality of nucleic acid probes comprises one or more probes configured to target said one or more elements of said bacterial 16S ribosomal RNA gene.