CLAIMS

WHAT IS CLAIMED IS:

1. A method of identifying a treatment for a disease of a subject, comprising:

(a) providing a biological sample of a subject comprising one or more microbial extracellular vesicles;

(b) enriching said one or more microbial extracellular vesicles with one or more affinity reagents, thereby generating one or more enriched microbial extracellular vesicles;

(c) detecting one or more molecular analytes from said one or more enriched microbial extracellular vesicles; and

(d) identifying said treatment for said disease of said subject based on said one or more molecular analytes.

2. The method of claim 1, wherein said biological sample comprises non-microbial extracellular vesicles and said one or more microbial extracellular vesicles.

3. The method of claim 2, wherein said one or more molecular analytes of said non-microbial extracellular vesicles comprise vesicle-associated cell-free non-microbial DNA, cell-free non-microbial RNA, non-microbial DNA, non-microbial RNA, non-microbial proteins, non-microbial metabolites, non-microbial lipids, non-microbial glycans, or any combination thereof.

4. The method of claim 1, wherein said one or more affinity reagents comprise recombinant innate immunity pattern recognition receptors or one or more antibodies, wherein said one or more antibodies comprise polyclonal antibodies, monoclonal antibodies, recombinant antibodies, aptamers, single-chain variable fragment (scFv), single-chain antibodies, or any combination thereof.

5. The method of claim 4, wherein said recombinant innate immunity pattern recognition receptors comprise Toll-like receptor 1 (TLR1, CD281), Toll-like receptor 2 (TLR2, CD282), Toll-like receptor 4 (TLR4, CD284), Toll-like receptor 5 (TLR5), Toll-like receptor 6 (TLR6, CD286), Toll-like receptor 10 (TLR10, CD290), CD14, Lipopolysaccharide binding protein,

Dectin-1, Dectin-2, Mannose Receptor (CD206), DC-SIGN, SIGNR1, Langerin, mannose binding lectin, ficolin-1, ficolin-2, ficolin-3, any combination thereof, or any derivatives thereof.

6. The method as in any of claim 1, wherein said enriching comprises:

(a) contacting said biological sample with said one or more affinity reagents to form capture reagent-molecular motif interaction complexes;

(b) contacting said capture reagent-molecular motif interaction complexes with a support; and

(c) separating said support from said biological sample to concentrate said capture reagent-molecular motif interaction complexes.

7. A method of identifying a treatment for a disease of a subject, comprising:

(a) providing a biological sample of a subject comprising one or more microbial extracellular vesicles and one or more non-microbial extracellular vesicles;

(b) enriching said one or more microbial extracellular vesicles with one or more first affinity reagents and said one or more non-microbial extracellular vesicles with one or more second affinity reagents, thereby generating one or more enriched microbial extracellular vesicles and one or more enriched non-microbial extracellular vesicles;

(c) detecting a first abundance of one or more molecular analytes from said enriched one or more microbial extracellular vesicles and a second abundance of one or more molecular analytes from said enriched one or more non-microbial extracellular vesicles; and

(d) identifying said treatment for said disease of said subject from an association between a combination of said first abundance of one or more molecular analytes and said second abundance of one or more molecular analytes, and a model of disease treatments associated with a third abundance of one or more molecular analytes from one or more microbial extracellular vesicles and a fourth abundance of one or more molecular analytes from one or more non-microbial extracellular vesicles.

8. The method of claim 7, wherein said one or more first affinity reagents or said one or more second affinity reagents comprise recombinant innate immunity pattern recognition receptors or one or more antibodies, wherein said one or more antibodies comprise polyclonal

antibodies, monoclonal antibodies, recombinant antibodies, and aptamers, single-chain variable fragment (scFv), single-chain antibodies or any combination thereof.

9. The method of claim 8, wherein said recombinant innate immunity pattern recognition receptors comprise Toll-like receptor 1 (TLR1, CD281), Toll-like receptor 2 (TLR2, CD282), Toll-like receptor 4 (TLR4, CD284), Toll-like receptor 5 (TLR5), Toll-like receptor 6 (TLR6, CD286), Toll-like receptor 10 (TLR10, CD290), CD14, Lipopolysaccharide binding protein, Dectin-1, Dectin-2, Mannose Receptor (CD206), DC-SIGN, SIGNR1, Langerin, mannose binding lectin, ficolin-1, ficolin-2, ficolin-3, or any derivatives thereof.

10. A method of training a predictive model, comprising:

(a) providing a biological sample of one or more subjects comprising one or more microbial extracellular vesicles, and an associated health classification of said one or more subjects;

(b) enriching said one or more microbial extracellular vesicles with one or more affinity reagents, thereby generating one or more enriched microbial extracellular vesicles;

(c) detecting one or more molecular analytes from said enriched one or more microbial extracellular vesicles; and

(d) training said predictive model with said one or more molecular analytes and said associated health classification of said one or more subjects.

11. The method of claim 10, wherein said biological sample comprises non-microbial extracellular vesicles.

12. The method of claim 10, wherein said one or more affinity reagents are configured to couple to one or more microbial cell wall molecular motifs or one or more non-microbial cell wall molecular motifs.

13. The method of claim 12, wherein said one or more microbial cell wall molecular motifs or said one or more non-microbial cell wall molecular motifs comprise canonical cell wall components such as lipopolysaccharides (LPS), lipoproteins, lipopeptides, lipoteichoic acid

(LTA), lipoarabinomannan, chitin, beta-glucans, zymosan, and glycosylphosphatidylinositol (GPI)-anchored proteins or any combinations thereof.

14. The method of claim 10, wherein said one or more affinity reagents comprise recombinant innate immunity pattern recognition receptors or one or more antibodies, wherein said one or more antibodies comprise polyclonal antibodies, monoclonal antibodies, recombinant antibodies, aptamers, single-chain variable fragment (scFv), single-chain antibodies, or any combination thereof.

15. The method of claim 14, wherein said recombinant innate immunity pattern recognition receptors comprise Toll-like receptor 1 (TLR1, CD281), Toll-like receptor 2 (TLR2, CD282), Toll-like receptor 4 (TLR4, CD284), Toll-like receptor 5 (TLR5), Toll-like receptor 6 (TLR6, CD286), Toll-like receptor 10 (TLR10, CD290), CD14, Lipopolysaccharide binding protein, Dectin-1, Dectin-2, Mannose Receptor (CD206), DC-SIGN, SIGNR1, Langerin, mannose binding lectin, ficolin-1, ficolin-2, ficolin-3, any combination thereof, or any derivatives thereof.

16. The method of claim 10, wherein said enriching comprises:

(a) contacting said liquid biological sample with said one or more affinity reagents to form capture reagent-molecular motif interaction complexes;

(b) contacting said capture reagent-molecular motif interaction complexes with a support; and

(c) separating said support from said liquid biological sample to concentrate said capture reagent-molecular motif interaction complexes.

17. A computer-implemented method of training a predictive model, comprising:

(a) receiving one or more subjects' biological sample sequencing data and corresponding health classifications from a database, wherein said biological sample sequencing data comprises sequences of one or more analytes of one or more microbial extracellular vesicles; and

(b) training said predictive model with said biological sample sequencing data and said corresponding health classification of said one or more subjects.

18. A computer system configured to identify a disease of a subject, comprising:

(a) one or more processors; and

(b) a non-transient computer readable storage medium including software, wherein said software comprises executable instruction that, as a result of execution, cause said one or more processors of said computer system to:

(i) receive a biological sample of a subject comprising one or more microbial extracellular vesicles;

(ii) enrich said one or more microbial extracellular vesicles with one or more affinity reagents;

(iii) detect one or more molecular analytes from said one or more microbial extracellular vesicles; and

(iv) identify said disease of said subject based on said one or more molecular analytes obtained from said one or more microbial extracellular vesicles.

19. A method of identifying a disease of a subject, comprising:

(a) providing a biological sample from a subject comprising one or more microbial extracellular vesicles;

(b) enriching said one or more microbial extracellular vesicles with one or more affinity reagents;

(c) detecting one or more molecular analytes from said one or more microbial extracellular vesicles; and

(d) identifying said disease of said subject based on said one or more molecular analytes from said one or more microbial extracellular vesicles.

20. The method of claim 1, wherein said biological sample comprises non-microbial extracellular vesicles.

21. The method of claim 1, wherein said one or more molecular analytes of said one or more microbial extracellular vesicles comprise vesicle-associated cell-free microbial DNA, cell-free

microbial RNA, microbial DNA, microbial RNA, microbial proteins, microbial metabolites, microbial lipids, microbial glycans, or any combination thereof.

22. A method of identifying a disease of a subject comprising:

(a) providing biological sample of a subject comprising one or more microbial extracellular vesicles and one or more non-microbial extracellular vesicles;

(b) enriching said one or more microbial extracellular vesicles with one or more first affinity reagents and said one or more non-microbial extracellular vesicles with one or more second affinity reagents, thereby generating one or more enriched microbial extracellular vesicles and one or more enriched non-microbial extracellular vesicles;

(c) detecting a first abundance of one or more molecular analytes from said enriched one or more microbial extracellular vesicles and a second abundance of one or more molecular analytes from said enriched one or more non-microbial extracellular vesicles; and

(d) identifying said disease of said subject from an association between a combination of said first abundance of one or more molecular analytes and said second abundances of one or more molecular analytes, and a model of diseases associated with a third abundance of one or more molecular analytes from one or more microbial extracellular vesicles and a fourth abundance of one or more molecular analytes from one or more non-microbial extracellular vesicles.