CLAIMS

WHAT IS CLAIMED IS:

1. A method for analyzing a biological sample from a subject, comprising:
   (a) assaying said biological sample from said subject to identify proteins in said biological sample to obtain proteomic information of said biological sample;
   (b) analyzing nucleic acid molecules from said biological sample to identify genotypic information of said biological sample; and
   (c) based on said proteomic information and said genotypic information, identifying a peptide variant or a genomic variant of said subject, wherein said peptide variant or said genomic variant is not otherwise identifiable in (a) or (b), respectively.
2. The method of claim 1, wherein (a) comprises subjecting said biological sample to an assay that identifies said proteins in said biological sample.
3. The method of claim 1 or 2, wherein (a) comprises contacting said biological sample with a particle under conditions sufficient for adsorption of said proteins from said biological sample to said particle.
4. The method of claim 3, wherein said proteins comprise a compressed dynamic range on said particle.
5. The method of claim 4, wherein said particle comprises a plurality of particles with different physicochemical properties.
6. The method of claim 5, wherein said plurality of particles comprises at least two of: silica coated SPION, PDMAPMA-polymer functionalized nanoparticles, glucose-6-phosphate functionalized nanoparticles, polystyrene carboxyl functionalized nanoparticles, dextran functionalized nanoparticles, mixed amide and carboxylate functionalized silica coated nanoparticles, tri-amine functionalized nanoparticles, di-amine functionalized nanoparticles, or mono-amine functionalized nanoparticles.
7. The method of claim 5, wherein said plurality of particles comprises at least two of: silica coated SPION, PDMAPMA-polymer functionalized nanoparticles, glucose-6-phosphate functionalized nanoparticles, polystyrene carboxyl functionalized nanoparticles, dextran functionalized nanoparticles, mixed amide and carboxylate functionalized silica coated nanoparticles, N-(3-Trimethoxysilylpropyl)diethylenetriamine coated nanoparticles, N^1-(3-(trimethoxysilyl)propyl)hexane-1,6-diamine functionalized nanoparticles, or 1,6-hexanediamine functionalized nanoparticles.

8. The method of claim 6, wherein a first subset of proteins of said proteins adsorbed by a first particle of said plurality of particles comprises at most 80% of types of proteins in common with a second subset of proteins of said proteins adsorbed by a second particle of said plurality of particles.

9. The method of claim 3, wherein said proteins comprise about 50 to 500 types of proteins or protein groups.

10. The method of any one of claims 6-8, wherein said proteins comprise about 250 to 25000 types of proteins or protein groups.

11. The method of any one of claim 1-10, wherein said subject comprises one subject.

12. The method of any one of claim 1-10, wherein said subject comprises a plurality of subjects.

13. The method of any one of claims 8-12, wherein said proteins comprise from 0.2% to 2% of said types of proteins in said biological sample.

14. The method of any one of claims 1-13, wherein (a) comprises identifying an abundance of said proteins in said biological sample.

15. The method of any one of claims 1-14, wherein said nucleic acid molecules comprise a cell-free deoxyribonucleic acid (cfDNA), a cell-free ribonucleic acid (cfRNA), or any combination thereof.

16. The method of claim 15, wherein (b) comprises identifying said nucleic acid molecules as comprising genomic DNA, mitochondrial DNA (mtDNA), circulating tumor DNA (ctDNA), or any combination thereof.

17. The method of claim 16, wherein (b) comprises identifying a cell type, a cancer type, a cancer stage, or any combination thereof of said ctDNA.

18. The method of any one of claims 1-17, wherein said nucleic acid molecules are derived from an exosome, an apoptotic body, a tumor cell, a healthy cell, a virtosome, an extracellular membrane vesicle, a neutrophil extracellular trap (NET), or any combination thereof.

19. A method for analyzing a biological sample from a subject, comprising:

(a) analyzing nucleic acid molecules in said biological sample from said subject to identify a cell type from which said nucleic acid molecules originated; and

(b) quantitating protein abundances for a plurality of proteins in said biological sample associated with said cell type.

20. The method of claim 19, further comprising obtaining sequences of said nucleic acid molecules to identify said genotypic information.

21. The method of claim 20, wherein said obtaining said sequences comprises fluorescence in situ hybridization (FISH), array-Comparative Genomic Hybridization (array-CGH), quantitative fluorescence PCR (QF-PCR), nanopore sequencing, sequencing by hybridization, sequencing by synthesis, sequencing by ligation, or any combination thereof.

22. The method of any one of claims 19-21, said quantitating said protein abundances comprises contacting said biological sample with a particle, thereby forming a biomolecule corona on said particle comprising said plurality of proteins.

23. The method of claim 22, wherein said plurality of proteins comprises a compressed dynamic range within said biomolecule corona.

24. The method of claim 22 or 23, wherein said biomolecule corona comprises one or more high abundance proteins having a reduced abundance than an abundance in said biological sample.

25. The method of any one of claims 22-24, wherein said particle comprises a plurality of particles comprising different physicochemical properties.

26. The method of claim 25, wherein said plurality of particles comprises at least two of: silica coated SPION, PDMAPMA-polymer functionalized nanoparticles, glucose-6-phosphate functionalized nanoparticles, polystyrene carboxyl functionalized nanoparticles, dextran functionalized nanoparticles, mixed amide and carboxylate functionalized silica coated nanoparticles, tri-amine functionalized nanoparticles, di-amine functionalized nanoparticles, or mono-amine functionalized nanoparticles.

27. The method of claim 25, wherein said plurality of particles comprises at least two of: silica coated SPION, PDMAPMA-polymer functionalized nanoparticles, glucose-6-phosphate functionalized nanoparticles, polystyrene carboxyl functionalized nanoparticles, dextran functionalized nanoparticles, mixed amide and carboxylate functionalized silica coated nanoparticles, N-(3-Trimethoxysilylpropyl)diethylenetriamine coated nanoparticles, N^1-(3-(trimethoxysilyl)propyl)hexane-1,6-diamine functionalized nanoparticles, or 1,6-hexanediamine functionalized nanoparticles.

28. The method of any one of claims 22-24, wherein said proteins comprise about 50 to 500 types of proteins or protein groups.

29. The method of any one of claims 25-27, wherein said proteins comprise about 250 to 25000 types of proteins or protein groups.

30. The method of any one of claim 19-29, wherein said subject comprises one subject.

31. The method of any one of claim 19-29, wherein said subject comprises a plurality of subjects.

32. The method of claim 28-31, wherein said plurality of proteins comprises at least 2% of said types of proteins in said biological sample.

33. The method of any one of claims 19-32, wherein said quantitating said protein abundances comprises identifying a splicing variant, a conformation, a post-translational modification, a cofactor association, or a substrate association of said plurality proteins.

34. A method for fractionating a biological sample from a subject, comprising:
    (a) contacting said biological sample with a plurality of particles to form, on said plurality of particles, biomolecule coronas comprising proteins and nucleic acid molecules from said biological sample; and
    (b) separating at least a subset of said biomolecule coronas from said biological sample, thereby fractionating said biological sample.

35. A method for analyzing a biological sample from a subject, comprising:
    (a) assaying proteins in said biological sample from said subject to identify signals assignable to a first plurality of proteins or protein fragments;
    (b) assaying nucleic acid molecules in said biological sample for nucleic acid sequence data, thereby identifying a second plurality of proteins or protein fragments associated with said nucleic acid sequences; and
    (c) identifying, from said first plurality of proteins or protein fragments, one or more proteins in said biological sample, wherein said one or more proteins is otherwise unidentifiable in the absence of said nucleic acid sequence data.

36. The method of claim 35, wherein said assaying said proteins comprises adsorbing said proteins to a particle.

37. The method of claim 35 or 36, wherein said adsorbing said proteins to said particle compresses a dynamic range of said proteins.

38. The method of any one of claims 35-37, wherein said assaying said nucleic acid molecules comprises sequencing.

39. The method of any one of claims 35-38, wherein said identifying comprises identifying a signal associated with said one or more proteins and which overlaps a signal of said signals assignable to said first plurality of proteins.

40. A method for processing a biological sample from a subject, comprising:

(a) assaying nucleic acid molecules in said biological sample from said subject for nucleic acid sequences of said nucleic acid molecules or fragments thereof;

(b) computer processing said nucleic acid sequences to generate data comprising protein sequences of proteins associated with said nucleotide sequences;

(c) assaying said biological sample for signals assignable to at least a subset of said proteins; and

(d) identifying, from said at least said subset of said proteins, a protein based at least partially on said data generated in (b).

41. The method of claim 40, wherein said assaying of (c) comprises contacting said biological sample with a particle, thereby forming a biomolecule corona on said particle comprising said at least said subset of said proteins.

42. The method of claim 40 or 41, wherein said signals assignable to said at least said subset of said proteins comprises at least 100,000 signals.

43. The method of any one of claims 40-42, wherein said identifying comprises identifying a splicing variant from among said at least said subset of said proteins.

44. The method of claim 43, wherein said identifying said splicing variant comprises identifying an abundance ratio of a plurality of splicing variants.

45. The method of any one of claims 42-44, wherein said signals assignable to said at least said subset of said proteins comprises a plurality of overlapping signals, and wherein said identifying comprises determining an intensity of an overlapping signal of said plurality of overlapping signals from a protein of said at least said subset of said proteins.

46. A method for assaying a biological sample, comprising:

(a) providing a dry composition comprising a surface modified particle and a support agent, said surface modified particle having a physicochemical property for variably selective adsorption of a plurality of biomolecules or biomolecule groups;

(b) reconstituting said dry composition in a liquid; and

(c) contacting said biological sample with said dry composition reconstituted in (b) to adsorb, on a surface of said surface modified particle, at least a portion of said biomolecules or biomolecule groups.

47. The method of claim 46, wherein said biomolecules or biomolecule groups comprise proteins or protein groups.

48. The method of claim 47, wherein said proteins or protein groups have a dynamic range of at least 7 orders of magnitude in concentration in said biological sample.

49. The method of either claim 47 or 48, wherein said proteins or protein groups have a dynamic range of at least 8 orders of magnitude in concentration in said biological sample.

50. The method of any one of claims 46-49, wherein said biological sample comprises plasma, serum, CSF, urine, tear, cell lysates, tissue lysates, cell homogenates, tissue homogenates, needle aspirates, fecal samples, synovial fluid, whole blood, saliva, or a combination thereof.

51. The method of any one of claims 46-50, wherein said dry composition is in a lyophilized bead format.

52. The method of any one of claims 46-51, wherein said dry composition comprises a plurality of particles comprising said surface modified particles.

53. The method of any one of claims 46-52, wherein said surface modified particle after (c) adsorbs at least 90% of biomolecules in said biological sample that the same surface modified particle dissolved in said liquid in the absence of lyophilization would adsorb from said biological sample.

54. The method of any one of claims 46-53, wherein said variably selective adsorption comprises low binding affinity, slow binding kinetics, or both.

55. The method of any one of claims 46-54, wherein said variably selective adsorption comprises an interaction that is not a protein-ligand interaction.

56. A method for assaying a biofluidic sample, comprising:

(a) providing a dry composition comprising a surface modified particle and a lyophilized support agent, said surface modified particle having an affinity for a plurality of biomolecules or biomolecule groups; and

(b) contacting said biofluidic sample with said dry composition in the absence of reconstitution of said dry composition to adsorb, on surfaces of said surface modified particle, at least a portion of said biomolecules or biomolecule groups.

57. The method of claim 56, wherein said biofluidic sample is diluted in a buffer solution before (b) at a volume ratio of about 1 part biofluidic sample to at least about 1 part buffer solution.

58. The method of claim 56 or 57, wherein said dry composition comprises a plurality of particles comprising said surface modified particles.

59. The method of claim 58, wherein said plurality of particles comprises at least two or more distinct particle types.

60. The method of claim 59, wherein said plurality of particles comprises at least two of: silica coated SPION, PDMAPMA-polymer functionalized nanoparticles, glucose-6-phosphate functionalized nanoparticles, polystyrene carboxyl functionalized nanoparticles, dextran functionalized nanoparticles, mixed amide and carboxylate functionalized silica coated nanoparticles, tri-amine functionalized nanoparticles, di-amine functionalized nanoparticles, or mono-amine functionalized nanoparticles.

61. The method of claim 59, wherein said plurality of particles comprises at least two of: silica coated SPION, PDMAPMA-polymer functionalized nanoparticles, glucose-6-phosphate functionalized nanoparticles, polystyrene carboxyl functionalized nanoparticles, dextran functionalized nanoparticles, mixed amide and carboxylate functionalized silica coated nanoparticles, N-(3-Trimethoxysilylpropyl)diethylenetriamine coated nanoparticles, N^1-(3-(trimethoxysilyl)propyl)hexane-1,6-diamine functionalized nanoparticles, or 1,6-hexanediamine functionalized nanoparticles.

62. The method of any one of claims 56-61, wherein said surface modified particle does not comprise an antibody, a T cell receptor, a chimeric antigen receptor, a receptor protein, or a variant or fragment thereof.

63. The method of any one of claims 56-62, further comprising, prior to (a), generating a solution or suspension comprising said surface modified particle and said support agent.

64. The method of any one of claims 63, further comprising flash freezing said solution or suspension to produce a frozen composition.

65. The method of either claim 64, further comprising lyophilizing said frozen composition to produce said dry composition.

66. A system for assaying a biological sample, comprising:
a substrate comprising a dry composition which comprises a particle and a support agent;
a sample storage unit comprising a biological sample;
a loading unit that is operably coupled to said substrate and said sample storage unit; and

a computer readable medium comprising machine-executable code that, upon execution by a processor, implements a method comprising:

(a) transferring said biological sample or a portion thereof from said sample storage unit to said substrate using said loading unit; and

(b) directing said biological sample into contact with said dry composition to produce a biomolecule corona comprising a plurality of biomolecules or biomolecule groups.

67. The system of claim 66, wherein said method further comprises lysing a species of said biological sample prior to (b) to produce a lysate.

68. The system of claim 67, wherein said method further comprises at least one of: reducing said lysate, filtering said lysate, alkylating said lysate.

69. The system of any one of claims 66-68, wherein said method further comprises at least one of: denaturing said biomolecule corona after (b) to produce denatured biomolecule corona, digesting said biomolecule corona after (b) to produce a digested biomolecule corona, eluting said biomolecule corona after (b), and separating using solid phase extraction after (b).

70. The system of any one of claims 66-69, wherein said method further comprises performing mass-spectrometry on said biomolecule corona after (b).

71. The system of any one of claims 66-70, wherein said substrate comprises a plasticware, and wherein said method further comprises providing a set of barcodes comprising at least a plasticware barcode, a particle barcode, and a reagent barcode and communicating said set of barcodes to said computer readable medium.

72. The system of any one of claims 66-71, wherein said method comprises separating at least a portion of said dry composition from at least a portion of said biological sample, wherein said separating comprises magnetic separation.

73. A dry particle formulation, comprising: a dry composition comprising (i) a particle comprising a surface modification for adsorption of a plurality of biomolecules or biomolecule groups and (ii) a support agent, wherein said dry composition is stable at a temperature of greater than 25°C for at least 3 months.

74. The dry particle formulation of claim 73, wherein said surface modification comprises a silica coating, a PDMAPMA-polymer functionalization, a glucose-6-phosphate functionalization, a polystyrene carboxyl functionalization, a dextran functionalization, an amide functionalization, a carboxyl functionalization, a tri-amine functionalization, a diamine functionalization, a mono-amine surface functionalization, or any combination thereof.

75. The dry particle formulation of claim 73, wherein said surface modification comprises a N-(3-Trimethoxysilylpropyl)diethylenetriamine functionalization, 1,6-hexanediamine functionalization, N1-(3-(trimethoxysilyl)propyl)hexane-1,6-diamine, or any combination thereof.

76. The dry particle formulation of any one of claims 73-75, wherein said surface modification comprises a metal oxide coating.

77. The dry particle formulation of any one of claims 73-76, wherein said surface modification comprises at least one exposed primary amine group, secondary amine group, tertiary amine group.

78. The dry particle formulation of any one of claims 73-77, wherein said surface modification comprises at least one monosaccharide.

79. The dry particle formulation of any one of claims 73-78, wherein said support agent comprises at least one of sucrose, d-mannitol, trehalose, glycerol, dextran, PEG, glucose, lactose, polysorbate, or amino acid.

80. The dry particle formulation of any one of claims 73-79, wherein said temperature is between 25 °C and 60 °C.

81. The dry particle formulation of any one of claims 73-80, wherein said particle, upon reconstitution of said dry composition in a solution, has a mean zeta potential that is between 85% to 115% of the zeta potential of a same particle dissolved in a same solution in the absence of lyophilization, as determined by zeta potential measurements.

82. The dry particle formulation of any one of claims 73-81, wherein upon reconstitution of said dry composition in a solution, said particle has a mean diameter that is between 85% to 115% of the mean diameter of a same particle dissolved in a same solution in the absence of lyophilization, as determined by dynamic light scattering (DLS).

83. The dry particle formulation of any one of claims 73-82, wherein said dry particle formulation comprises a plurality of particles comprising at least two of: silica coated SPION, PDMAPMA-polymer functionalized nanoparticles, glucose-6-phosphate functionalized nanoparticles, polystyrene carboxyl functionalized nanoparticles, dextran functionalized nanoparticles, mixed amide and carboxylate functionalized silica coated nanoparticles, tri-amine functionalized nanoparticles, di-amine functionalized nanoparticles, or mono-amine functionalized nanoparticles.

84. The dry particle formulation of any one of claims 73-83, wherein said dry particle formulation comprises a plurality of particles comprising at least two of: silica coated SPION, PDMAPMA-polymer functionalized nanoparticles, glucose-6-phosphate functionalized nanoparticles, polystyrene carboxyl functionalized nanoparticles, dextran functionalized nanoparticles, mixed amide and carboxylate functionalized silica coated nanoparticles, N-(3-Trimethoxysilylpropyl)diethylenetriamine coated nanoparticles, N^1-(3-(trimethoxysilyl)propyl)hexane-1,6-diamine functionalized nanoparticles, or 1,6-hexanediamine functionalized nanoparticles.

85. A kit comprising the dry particle formulation of any one of claims 73-84 and a substrate configured to receive and retain said dry composition.

86. A dry particle formulation, comprising: a dry composition comprising a particle which is surface modified for adsorption of a plurality of biomolecules or biomolecule groups, and a support agent, wherein said dry composition is configured for subsequent use without reconstitution in a solvent.

87. The dry particle formulation of claim 86, wherein said dry composition is stable at a temperature of greater than 37 °C for at least 7 days.

88. The dry particle formulation of claim 86, wherein said dry composition is stable at 37 °C for at least 40 days.

89. The dry particle formulation of any one of claims 86-88, wherein said particle is a lyophilized particle.

90. The dry particle formulation of any one of claims 89, wherein said lyophilized particle, upon reconstitution of said dry composition, has a particle size that is between 85% to 115% of the size of a same particle dissolved in a solution in the absence of lyophilization, as determined by dynamic light scattering (DLS).

91. The dry particle formulation of claim 89 or 90, wherein said lyophilized particle, upon reconstitution of said dry composition, has a zeta potential that is between 85% to 115% of the zeta potential of a same particle dissolved in a solution in the absence of lyophilization, as determined by zeta potential measurements.

92. The dry particle formulation of any one of claims 86-91, wherein said dry particle formulation comprises a plurality of particles comprising at least two of: silica coated SPION, PDMAPMA-polymer functionalized nanoparticles, glucose-6-phosphate functionalized nanoparticles, polystyrene carboxyl functionalized nanoparticles, dextran

functionalized nanoparticles, mixed amide and carboxylate functionalized silica coated nanoparticles, tri-amine functionalized nanoparticles, di-amine functionalized nanoparticles, or mono-amine functionalized nanoparticles.

93. The dry particle formulation of any one of claims 86-91, wherein said dry particle formulation comprises a plurality of particles comprising at least two of: silica coated SPION, PDMAPMA-polymer functionalized nanoparticles, glucose-6-phosphate functionalized nanoparticles, polystyrene carboxyl functionalized nanoparticles, dextran functionalized nanoparticles, mixed amide and carboxylate functionalized silica coated nanoparticles, N-(3-Trimethoxysilylpropyl)diethylenetriamine coated nanoparticles, N^1-(3-(trimethoxysilyl)propyl)hexane-1,6-diamine functionalized nanoparticles, or 1,6-hexanediamine functionalized nanoparticles.

94. A kit comprising a dry particle formulation of any one of claims 86-93 and a substrate configured to receive and retain said dry composition.

WHAT IS CLAIMED IS:

1. A method for analyzing a biological sample from a subject, comprising:

(a) assaying said biological sample from said subject to identify proteins in said biological sample to obtain proteomic information of said biological sample, wherein said proteomic information comprises signals assignable to a first plurality of proteins or protein fragments of said proteins in said biological sample;

(b) analyzing nucleic acid molecules from said biological sample to identify genotypic information of said biological sample, wherein said genotypic information comprises signals assignable to a second plurality of proteins or protein fragments associated with said nucleic acid molecules; and

(c) based on said proteomic information and said genotypic information, identifying a peptide variant or a genomic variant of said subject, wherein said peptide variant or said genomic variant is not otherwise identifiable in (a) or (b), respectively, wherein said identifying comprises identifying said peptide variant or said genomic variant based at least in part on a signal of said genotypic information which overlaps with a signal of said proteomic information.

2. The method of claim 1, wherein said signal of said proteomic information overlaps with another signal of said proteomic information, wherein said another signal is assignable to another protein or protein fragment.

3. The method of claim 1, wherein said signal of said genotypic information overlaps with another signal of said genotypic information, wherein said another signal of said genotypic information is assignable to another genomic variant or a nucleic acid sequence of a reference genome corresponding to said another genomic variant.

4. The method of claim 1, wherein (a) comprises subjecting said biological sample to an assay that identifies said proteins in said biological sample.

5. The method of claim 1, wherein (a) comprises contacting said biological sample with a particle under conditions sufficient for adsorption of said proteins from said biological sample to said particle.

6. The method of claim 5, wherein said proteins comprise a compressed dynamic range on said particle.

7. The method of claim 6, wherein said proteins comprise a concentration range of at least 6 orders of magnitude in said biological sample.

8. The method of claim 6, wherein said particle comprises a plurality of particles with different physicochemical properties.

9. The method of claim 8, wherein a first subset of proteins of said proteins adsorbed by a first particle of said plurality of particles comprises at most 80% of types of proteins in common with a second subset of proteins of said proteins adsorbed by a second particle of said plurality of particles.

10. The method of claim 5, wherein said proteins in said biological sample comprise about 250 to 25000 types of proteins or protein groups.

11. The method of claim 1, wherein said subject comprises one subject.

12. The method of claim 1, wherein said subject comprises a plurality of subjects.

13. The method of claim 9, wherein said proteins in said sample comprise from 0.2% to 2% of said types of proteins in said biological sample.

14. The method of claim 1, wherein (a) comprises identifying an abundance of said proteins in said biological sample.

15. The method of claim 1, wherein said nucleic acid molecules comprise a cell-free deoxyribonucleic acid (cfDNA), a cell-free ribonucleic acid (cfRNA), or any combination thereof.

16. The method of claim 15, wherein (b) comprises identifying said nucleic acid molecules as comprising genomic DNA, mitochondrial DNA (mtDNA), circulating tumor DNA (ctDNA), or any combination thereof.

17. The method of claim 16, wherein (b) comprises identifying a cell type, a cancer type, a cancer stage, or any combination thereof of said ctDNA.

18. The method of claim 1, wherein said nucleic acid molecules are derived from an exosome, an apoptotic body, a tumor cell, a healthy cell, a virtosome, an extracellular membrane vesicle, a neutrophil extracellular trap (NET), or any combination thereof.

19. The method of claim 1, further comprising obtaining sequences of said nucleic acid molecules to identify said genotypic information.

20. The method of claim 1, wherein (c) comprises identifying a splicing variant, a conformation, a post-translational modification, a cofactor association, or a substrate association of a protein of said proteins in said biological sample based on said proteomic information and said genotypic information.