CLAIMS

WHAT WE CLAIM IS:

1. A method for ~~treating~~ assessing a likelihood of infertility in an individual ~~in need thereof~~ comprising:

   (a) determining by an assay a level of a first bacteria, ~~-~~ a level of a second bacteria, and/or a level of a miRNA~~, or both~~ in a sample from the individual; ~~and~~

   (b) comparing a ratio of the first bacteria to the second bacteria and/or the level of the miRNA in the sample to a cohort of control samples; and

   ~~(b)~~(c) determining the individual as having the likelihood of infertility if the ratio of the first bacteria to the second bacteria and/or the level of the miRNA in the sample is different from the cohort of control sample~~the sample has the level of the first bacteria, the level of the miRNA, or both, then administering a therapy to modulate a microbiome of the individual, thereby treating the infertility in the individual~~.

~~2. The method of claim 1, wherein step (a) comprises determining by an assay the level of the first bacteria and the level of the miRNA.~~

~~3.~~2. The method of claim 1, wherein the first bacteria and/or the second bacteria is selected from the group consisting of a Proteobacteria, an Actinobacteria, a Bacteroidetes, a Firmicutes, and any combination thereof.

~~4.~~3. The method of claim 1, wherein the first bacteria and/or the second bacteria is a species of a Proteobacteria, an Actinobacteria, a Bacteroidetes, or a Firmicutes.

~~5. The method of claim 1, wherein the first bacteria is selected from the group consisting of Lactobacillus iners, Lactobacillus brevis, a Firmicutes, a Bacteroidetes, a Proteobacteria, an Actinobacteria, and any combination thereof.~~

~~6. The method of any one of claims 1-5, wherein the method further comprises determining a level of a second bacteria.~~

~~7. The method of claim 6, wherein the second bacteria is selected from the group consisting of a Proteobacteria, an Actinobacteria, a Bacteroidetes, a Firmicutes, and any combination thereof.~~

~~8. The method of claim 6, wherein the second bacteria is a species of a Proteobacteria, an Actinobacteria, a Bacteroidetes, or a Firmicutes.~~

~~9. The method of claim 6, wherein the second bacteria is selected from the group consisting of~~

~~Lactobacillus iners, Lactobacillus brevis, a Firmicutes, a Bacteroidetes, a Proteobacteria, an Actinobacteria, and any combination thereof.~~

~~10. The method of any one of claims 6-9, further comprising determining a ratio of the first bacteria to the second bacteria.~~

~~11.~~4. The method of claim ~~10~~1, wherein the first bacteria is Lactobacillus iners and the second bacteria is Lactobacillus brevis.

~~12.~~5. The method of claim ~~10~~1, wherein the first bacteria is a Firmicutes and the second bacteria is a Bacteroidetes.

~~13. The method of any one of claims 1-12, wherein the miRNA is derived from a transcriptome of the individual.~~

~~14.~~6. The method of claim 1~~3~~, wherein the miRNA is derived from a transcriptome of the individual, or wherein the miRNA is selected from the group consisting of miR21-5p, miR155-5p, and any combination thereof.

~~15. The method of any one of claims 1-14, wherein the level of the first bacteria is decreased below a threshold level of the first bacteria derived from a cohort of control samples.~~

~~16. The method of claim 15, wherein the level of the first bacteria is decreased by at least about 0.25-fold below the threshold level.~~

~~17.~~7. The method of ~~any one of claims 1-16~~claim 1, wherein the level of the miRNA is elevated above a threshold level of the miRNA derived from ~~a~~the cohort of control samples.

~~18. The method of claim 17, wherein the level of the miRNA is elevated by at least about 2-fold above the threshold level.~~

~~19.~~8. The method of ~~any one of claims 10-18~~claim 1, wherein ~~a~~ the ratio of the first bacteria to the second bacteria is elevated above a threshold level of a ratio of the first bacteria to the second bacteria derived from ~~a~~ the cohort of control samples.

~~20. The method of claim 19, wherein the ratio of the first bacteria to the second bacteria is elevated by at least about 2-fold above the threshold level.~~

~~21.~~9. The method of ~~any one of claims 10-18~~claim 1, wherein the~~a~~ ratio of the first bacteria to the second bacteria is decreased below a threshold level of a ratio of the first bacteria to the second bacteria derived from the~~a~~ cohort of control samples.

~~22. The method of claim 21, wherein the ratio of the first bacteria to the second bacteria is~~

~~decreased by at least about 2-fold below the threshold level.~~

~~23.~~10. The method of ~~any one of claims 15-22~~claim 1, wherein the control samples are obtained from individuals that are fertile.

~~24.~~11. The method of ~~any one of claims 1-23~~claim 1, further comprising determining by an assay a level of an inflammatory biomarker, and wherein the ~~therapy is administered~~likelihood of infertility in the individual is determined in part based on ~~the level of the first bacteria, the level of the miRNA, and~~ the level of the inflammatory biomarker.

~~25.~~12. The method of claim ~~24~~11, wherein the inflammatory biomarker is associated with a disease or disorder selected from the group consisting of anemia, hypovitaminosis B, hypovitaminosis D, hypothyroidism, a metabolic syndrome, polycystic ovary syndrome, endometriosis, autoimmunity, and any combination thereof.

~~26.~~13. The method of claim ~~24~~11, wherein the inflammatory biomarker is selected from the group consisting of anti-thyroid peroxidase, thyroid antithyroglobulin antibody, anti-nuclear antibody, anti-Saccharomyces cerevisiae antibody IgA, anti-Saccharomyces cerevisiae antibody IgG, and any combination thereof.

~~27.~~14. The method of ~~any one of claims 1-26~~claim 1, wherein the ~~therapy~~ likelihood of infertility in the individual is determined in part based on the individual's medical history.

~~28.~~15. The method of ~~claim 27~~claim 14, wherein the individual's medical history comprises determining a glycidic metabolic component, a lipidic metabolic component, intestinal permeability, or body mass index of the individual.

~~29. The method of any one of claims 1-28, wherein the therapy is determined by the level of the first bacteria, a level of the second bacteria, the level of a miRNA, a ratio of the first bacteria to the second bacteria, or a level or presence of a biomarker.~~

~~30. The method of any one of claims 1-29, wherein the therapy is selected from a group of predetermined therapies consisting of administering a nutritional plan, administering a vitamin, a supplement, a probiotic, or any combination thereof~~

~~31. The method of claim 30, wherein the vitamin is selected from the group consisting of vitamin A, vitamin B12, vitamin C, vitamin D3, vitamin E, and any combination thereof.~~

~~32. The method of claim 30, wherein the probiotic is selected from the group consisting of Bifidobacterium longum, Bifidobacterium animalis subsp lactis, Bifidobacterium breve,~~

~~Lactobacillus rhamnosus, Lactobacillus brevis, Lactobacillus acidophilus, Lactobacillus casei, and any combination thereof.~~

~~33. The method of claim 30, wherein the supplement is selected from the group consisting of omega 3, trans-resveratrol, selenium, L-tryptophan, magnesium, vitamin D, vitamin A, vitamin B12, vitamin E, vitamin C, L-glutamine, and any combination thereof.~~

~~34. The method according to any one of claims 30-33, wherein the nutritional plan is administered for at least one week.~~

~~35. The method according to any one of claims 30-33, wherein the nutritional plan is administered for at least one month.~~

~~36.~~16. The method of ~~any one of claims 1-35~~claim 1, wherein the sample is selected from the group consisting of a saliva sample, a buccal sample, a blood sample, a urine sample, an anal sample, a vaginal sample, and any combination thereof.

~~37. The method of any one of claims 1-35, wherein the sample is selected from the group consisting of an anal sample, a vagina sample, a buccal sample, a blood sample, and any combination thereof.~~

~~38.~~17. The method of ~~any one of claims 1-37~~claim 1, wherein the assay is selected from the group consisting of quantitative real-time PCR, northern blot, RNA-seq, microarray, ELISA, homogenous protein assays, immunoblot, and mass spectrometry.

~~39. The method of any one of claims 1-38, wherein the individual is female.~~

~~40. The method of any one of claims 1-38, wherein the individual is male.~~

~~41. A method for assessing a likelihood of infertility in an individual comprising:~~

~~(a) determining a level of a first bacteria, a level of a miRNA, or both in a sample derived from the individual; and~~

~~(b) assessing the likelihood of infertility in the individual based on the level of the first bacteria, the level of the miRNA, or both,~~

18. ~~The method of claim 1,~~ wherein the miRNA provides an area under the curve (AUC) value of greater than about 0.8 in a receiver operating characteristic (ROC) curve analysis.

~~42. A method for sample preparation for assessing a likelihood of infertility in an individual comprising:~~

~~(a) providing a sample from the individual, wherein the sample comprises a first bacteria, a~~

~~miRNA, or both;~~

~~(b) lysing the sample thereby producing a lysed sample;~~

~~(c) performing a reverse transcription reaction on said lysed sample to obtain a lysed, reverse transcribed sample;~~

~~(d) performing an amplification reaction on the lysed, reverse transcribed sample to obtain an amplified biological sample, wherein said amplification reaction on said lysed, reverse transcribed sample is performed with a set of bacteria primers specific for a bacteria nucleic acid sequence, a set of miRNA primers specific for a miRNA nucleic acid sequence, or both, wherein the bacteria primers specific amplifies the bacteria nucleic acid sequence and the miRNA primers amplifies miRNA nucleic acid sequence; and~~

~~(e) sequencing the amplified sample using RNA sequencing or quantifying the first bacteria, the miRNA, or both in the amplified sample.~~

~~43. The method of any one of claims 41-42, wherein the first bacteria is selected from the group consisting of a Proteobacteria, an Actinobacteria, a Firmicutes, and any combination thereof.~~

~~44. The method of any one of claims 41-42, wherein the first bacteria is a species of a Proteobacteria, an Actinobacteria, a Bacteroidetes, or a Firmicutes.~~

~~45. The method of any one of claims 41-42, wherein the first bacteria is selected from the group consisting of Lactobacillus iners, Lactobacillus brevis, a Firmicutes, a Bacteroidetes, and any combination thereof.~~

~~46. The method of any one of claims 41-45, wherein the method further comprises determining a level of a second bacteria.~~

~~47. The method of claim 46, wherein the second bacteria is selected from the group consisting of a Proteobacteria, an Actinobacteria, a Firmicutes, and any combination thereof.~~

~~48. The method of claim 46, wherein the second bacteria is a species of a Proteobacteria, an Actinobacteria, a Bacteroidetes, or a Firmicutes.~~

~~49. The method of claim 46, wherein the second bacteria is selected from the group consisting of Lactobacillus iners, Lactobacillus brevis, a Firmicutes, a Bacteroidetes, and any combination thereof.~~

~~50. The method of any one of claims 46-49, further comprising determining a ratio of the first bacteria to the second bacteria.~~

~~51. The method of claim 50, wherein the first bacteria is Lactobacillus iners and the second~~

~~bacteria is Lactobacillus brevis.~~

~~52. The method of claim 50, wherein the first bacteria is a Firmicutes and the second bacteria is a Bacteroidetes.~~

~~53. The method of any one of claims 41-52, wherein the miRNA is derived from a transcriptome of the individual.~~

~~54. The method of claim 53, wherein the miRNA is selected from the group consisting of miR21-5p, miR155-5p, and any combination thereof.~~

~~55. The method of any one of claims 41-54, wherein the level of the first bacteria is decreased below a threshold level of the first bacteria derived from a cohort of control samples.~~

~~56. The method of claim 55, wherein the level of the first bacteria is decreased by at least about 0.25-fold below the threshold level.~~

~~57. The method of any one of claims 41-56, wherein the level of the miRNA is elevated above a threshold level of the miRNA derived from a cohort of control samples.~~

~~58. The method of claim 57, wherein the level of the miRNA is elevated by at least about 2-fold above the threshold level.~~

~~59. The method of any one of claims 50-58, wherein a ratio of the first bacteria to the second bacteria is elevated above a threshold level of a ratio of the first bacteria to the second bacteria derived from a cohort of control samples.~~

~~60. The method of claim 59, wherein the ratio of the first bacteria to the second bacteria is elevated by at least about 2-fold above the threshold level.~~

~~61. The method of any one of claims 50-58, wherein a ratio of the first bacteria to the second bacteria is decreased below a threshold level of a ratio of the first bacteria to the second bacteria derived from a cohort of control samples.~~

~~62. The method of claim 61, wherein the ratio of the first bacteria to the second bacteria is decreased by at least about 2-fold below the threshold level.~~

~~63. The method of any one of claims 55-62, wherein the control samples are obtained from individuals that are fertile.~~

~~64. The method of any one of claims 41-63, further comprising performing an assay of the sample to determine a level of an inflammatory biomarker~~

~~65. The method of claim 64, wherein the assessment is based on the level of the first bacteria, the~~

~~level of the miRNA, the level of the inflammatory biomarker, or any combination thereof.~~

~~66. The method of claim 64, wherein the assessment is based on the level of the first bacteria, the level of the miRNA, and the level of the inflammatory biomarker.~~

~~67. The method of any one of claims 64-66, wherein the inflammatory biomarker is associated with a disease or disorder selected from the group consisting of anemia, hypovitaminosis B, hypovitaminosis D, hypothyroidism, a metabolic syndrome, polycystic ovary syndrome, endometriosis, autoimmune disorder, and any combination thereof.~~

~~68. The method of claim 67, wherein the autoimmune disorder is selected from the group consisting of Celiac disease, Hashimoto's disease, Crohn´s disease, autoimmune diabetes, Lupus, Graves, rheumatoid arthritis, scleroderma, myasthenia gravis, and Sjogren.~~

~~69. The method of any one of claims 64-65, wherein the inflammatory biomarker is selected from the group consisting of anti-thyroid peroxidase, thyroid antithyroglobulin antibody, anti-nuclear antibody, anti-Saccharomyces cerevisiae antibody IgA, anti-Saccharomyces cerevisiae antibody IgG, and any combination thereof.~~

~~70. The method of any one of claims 41-69, further comprising determining the individual's medical history prior to step (c).~~

~~71. The method of claim 70, wherein the individual's medical history comprises determining a glycidic metabolic component, a lipidic metabolic component, intestinal permeability, or body mass index of the individual.~~

~~72. The method of any one of claims 41-71, further comprising, if a determination is made based on the level of the first bacteria and the level of the miRNA, then providing a nutritional plan to the individual.~~

~~73. The method of claim 72, wherein the nutritional plan comprises administering a vitamin, a supplement, a probiotic, or any combination thereof to the individual.~~

~~74. The method of claim 73, wherein the vitamin is selected from the group consisting of vitamin A, vitamin B12, vitamin C, vitamin D3, vitamin E, and any combination thereof.~~

~~75. The method of claim 73, wherein the probiotic is selected from the group consisting of Bifidobacterium longum, Bifidobacterium animalis subsp lactis, Bifidobacterium breve, Lactobacillus rhamnosus, Lactobacillus brevis, Lactobacillus acidophilus, Lactobacillus casei, and any combination thereof.~~

~~76. The method of claim 73, wherein the supplement is selected from the group consisting of omega 3, trans-resveratrol, selenium, L-tryptophan, magnesium, vitamin D, vitamin A, vitamin B12, vitamin E, vitamin C, L-glutamine, and any combination thereof.~~

~~77. The method according to any one of claims 72-76, wherein the nutritional plan is administered for at least one week.~~

~~78. The method according to any one of claims 72-76, wherein the nutritional plan is administered for at least one month.~~

~~79. The method of any one of claims 41-78, wherein the sample is selected from the group consisting of a saliva sample, a buccal sample, a blood sample, a urine sample, an anal sample, a vaginal sample, and any combination thereof.~~

~~80. The method of any one of claims 41-78, wherein the sample is selected from the group consisting of an anal sample, a vagina sample, a buccal sample, a blood sample, and any combination thereof.~~

~~81. The method of any one of claims 41-80, wherein the assay is selected from the group consisting of quantitative real-time PCR, northern blot, RNA-seq, microarray, ELISA, homogenous protein assays, immunoblot, and mass spectrometry.~~

~~82. The method of any one of claims 41-81, wherein the individual is female.~~

~~83.~~19. The method of ~~any one of claims 41-82~~claim 18, wherein the miRNA provides at least about an 80% sensitivity as determined by ROC curve analysis in assessing the likelihood of infertility in the individual.

~~84.~~20. The method of ~~any one of claims 41-83~~claim 18, wherein the miRNA provides an accuracy of at least about 80% as determined by ROC curve analysis in assessing the likelihood of infertility in the individual.

~~85. A kit comprising:~~

~~(a) one or more probes that bind to a first bacteria, a miRNA, or both;~~

~~(b) a first detecting reagent for detecting binding of the one or more probes to the first bacteria, the miRNA, or both; and~~

~~(c) instructions for use.~~

~~86. The kit of claim 85, wherein the first bacteria is selected from the group consisting of a Proteobacteria, an Actinobacteria, a Firmicutes, and any combination thereof.~~

87. The kit of claim 85, wherein the first bacteria is a species of a Proteobacteria, an Actinobacteria, a Bacteroidetes, or a Firmicutes.

88. The kit of claim 85, wherein the first bacteria is selected from the group consisting of Lactobacillus iners, Lactobacillus brevis, a Firmicutes, a Bacteroidetes, and any combination thereof.

89. The kit of any one of claims 85-88, wherein the kit further comprises one or more probes for detecting a level of a second bacteria.

90. The kit of claim 89, wherein the second bacteria is selected from the group consisting of a Proteobacteria, an Actinobacteria, a Firmicutes, and any combination thereof.

91. The kit of claim 89, wherein the second bacteria is a species of a Proteobacteria, an Actinobacteria, a Bacteroidetes, or a Firmicutes.

92. The kit of claim 89, wherein the second bacteria is selected from the group consisting of Lactobacillus iners, Lactobacillus brevis, a Firmicutes, a Bacteroidetes, and any combination thereof.

93. The kit of any one of claims 85-92, wherein the miRNA is selected from the group consisting of miR21-5p, miR155-5p, and any combination thereof.

94. A kit comprising

(a) a first collection component for collecting a blood sample;

(b) a second collection component for collecting a saliva sample;

(c) a third collection component for collecting a vaginal sample; and

(d) instructions for use.

95. The kit of claim 94, wherein the blood sample is analyzed for a biomarker selected from the group consisting of LDL, insulin, anti-nuclear antibody (ANA), vitamin D, vitamin B12, secretory IgA, miR155, miR21, and any combination thereof.

96. The kit of claim 94, wherein the blood sample is analyzed for a biomarker selected from the group consisting of LDL, insulin, anti-nuclear antibody (ANA), vitamin D, vitamin B12, and any combination thereof.

97. The kit of any one of claims 94-96, wherein the saliva sample is analyzed for a biomarker selected from the group consisting of LDL, insulin, anti-nuclear antibody (ANA), vitamin D, vitamin B12, secretory IgA, miR155, miR21, and any combination thereof.

98. The kit of any one of claims 94-96, wherein the saliva sample is analyzed for secretory IgA.

99. The kit of any one of claims 94-98, wherein the vaginal sample is analyzed for a biomarker

~~selected from the group consisting of LDL, insulin, anti-nuclear antibody (ANA), vitamin D, vitamin B12, secretory IgA, miR155, miR21, and any combination thereof.~~

~~100. The kit of any one of claims 94-98, wherein the vaginal sample is analyzed for a biomarker selected from the group consisting of miR155, miR21, and any combination thereof.~~