pharmaceutical toxicity. In some embodiments, the microbiome of a given individual may be unique with respect to the cancer treated. In some embodiments, the microbiome may be screened by isolating cell-free microbial nucleic acid compositions of DNA or RNA from a subject's liquid biopsy. In some embodiments, the microbial nucleic acid composition may be determined by nucleic acid sequencing techniques.

[**0003a**] In an aspect, the present disclosure provides a method for generating a therapeutic treatment prediction of one or more subjects, comprising: (a) receiving: i. one or more liquid biopsies of one or more subjects, wherein said one or more liquid biopsies comprise one or more microbial and non-microbial nucleic acid compositions; ii. at least one therapeutic treatment of said one or more subjects; and iii. clinical metadata from said one or more subjects; (b) determining one or more sequences of said one or more microbial and non-microbial nucleic acid compositions of said one or more subjects; and (c) processing said one or more microbial and non-microbial nucleic acid compositions and said clinical metadata with a trained predictive model thereby generating said therapeutic treatment prediction of said one or more subjects, wherein said trained predictive model is trained with a plurality of microbial and non-microbial nucleic acid compositions derived from a liquid biopsy sample of subjects with a corresponding therapeutic outcome and clinical metadata from said subjects.

[0004] Examples of the disclosure provided herein, in some embodiments, comprise a method for generating a predictive model, comprising: (a) receiving: (i) one or more liquid biopsies of a first set of one or more subjects, wherein said one or more liquid biopsies comprise one or more microbial and non-microbial nucleic acid compositions; and (ii) at least one therapeutic outcome of said first set of one or more subjects administered a therapeutic treatment; (b) determining one or more sequences of said one or more microbial and non-microbial nucleic acid compositions of said first set of one or more subjects; (c) determining a correlation between said first set of one or more subjects' said at least one therapeutic outcome and said one or more sequences of said one or more microbial and non-microbial nucleic acid compositions; and (d) generating a predictive model with said correlation, wherein said predictive model is configured to provide a prediction of at least one therapeutic outcome of a second set of one or more subjects when administered said therapeutic treatment based on an input to said predictive model of said second set of one or more subjects' one or more microbial and non-microbial nucleic acid composition one or more sequences, wherein said first set of one or more subjects is different than said second set of one or more subjects. In some embodiments, the first or second set of one or more

subjects' said at least one therapeutic outcome comprises therapeutic efficacy, therapeutic failure, therapeutic safety, therapeutic adverse side effect or any combination thereof. In some embodiments, the first or second set of one or more subjects' one or more microbial nucleic acid compositions comprise cell-free (cf) nucleic acids. In some embodiments, the first or second set of one or more subjects' one or more microbial nucleic acid compositions comprise microbial cell-free microbial DNA (cf-mbDNA), cell-free microbial RNA (cf-mbRNA) or any combination thereof. In some embodiments, the first or second set of one or more subjects' one or more microbial nucleic acid compositions comprise an origin of viral, bacterial, archaeal, fungal sources or any combination thereof. In some embodiments, the therapeutic treatment treats cancer. In some embodiments, the predictive model is used to analyze a therapeutic outcome of subjects treated for acute myeloid leukemia, adrenocortical carcinoma, bladder urothelial carcinoma, brain lower grade glioma, breast invasive carcinoma, cervical squamous cell carcinoma and endocervical adenocarcinoma,

lactation, exercise, comorbidities, occupational exposures, psychological status, other medications, or any combination thereof. In some embodiments, the predictive model is a machine learning model. In some embodiments, the predictive model is a regularized machine learning model. In some embodiments, the predictive model is a combination of one or more machine learning models. In some embodiments, the predictive model identifies and removes said first or second one or more subjects' one or more microbial or non-microbial nucleic acid compositions classified as noise while selectively retaining other said one or more microbial or non-microbial features termed signal. In some embodiments, the first or second set of one or more subjects are non-human mammal. In some embodiments, the first or second set of one or more subjects are human. In some embodiments, the said liquid biopsy comprises whole blood, plasma, serum, saliva, sputum, urine, cerebral spinal fluid, sweat, tears, exhaled breath condensate, stool, or any combination thereof.

[0005] Another example of the disclosure described herein, in some embodiments, comprises a method for generating a therapeutic treatment prediction of one or more subjects, comprising: (a) providing one or more biological samples of a first set of one or more subjects, wherein said first set of one or more subjects comprise a therapeutic treatment outcome when administered a therapeutic treatment; (b) sequencing said one or more microbial and non-microbial nucleic acid compositions of said first set of one or more subjects thereby generating one or more sequences; (c) training a predictive model with said first set of one or more subjects' microbial and non-microbial nucleic acid compositions said one or more sequences and said therapeutic treatment outcome, thereby producing a trained predictive model; and (d) generating a therapeutic treatment prediction for a second set of one or more subjects by inputting said second set of one or more subjects' one or more microbial and non-microbial nucleic compositions one or more sequences, clinical meta data, and said therapeutic treatment to be administered into said predictive model. In some embodiments, the therapeutic treatment treats cancer. In some embodiments, the first or second set of one or more subjects' one or more microbial nucleic acid compositions comprise cell-free (cf) nucleic acids. In some embodiments, the first or second set of one or more subjects' one or more microbial nucleic acid compositions comprise microbial cell-free microbial DNA (cf-mbDNA), cell-free microbial RNA (cf-mbRNA), or any combination thereof. In some embodiments, the first or second set of one or more subjects' one or more microbial nucleic acid compositions originate from viral, bacterial, archaeal, fungal sources or any combination thereof . In some embodiments, the therapeutic treatment prediction is used to triage therapeutic clinical trial subjects into responder, non-responder, non-adverse, and adverse

groups prior to therapeutic intervention. In some embodiments, the trained predictive model is used retrospectively. In some embodiments, the trained predictive model is utilized to longitudinally model the course of one or more cancers' response to therapy. In some embodiments, the predictive model is used to analyze said therapeutic treatment prediction of one or more subjects receiving treatment for acute myeloid leukemia, adrenocortical carcinoma, bladder urothelial carcinoma, brain lower grade glioma, breast invasive carcinoma, cervical squamous cell carcinoma and endocervical adenocarcinoma, cholangiocarcinoma, colon adenocarcinoma, esophageal carcinoma, glioblastoma multiforme, head and neck squamous cell carcinoma, kidney chromophobe, kidney renal clear cell carcinoma, kidney renal papillary cell carcinoma, liver hepatocellular carcinoma, lung adenocarcinoma, lung squamous cell carcinoma, lymphoid neoplasm diffuse large B-cell lymphoma, mesothelioma, ovarian serous cystadenocarcinoma, pancreatic adenocarcinoma, pheochromocytoma and paraganglioma, prostate adenocarcinoma, rectum adenocarcinoma, sarcoma, skin cutaneous melanoma, stomach adenocarcinoma, testicular germ cell tumors, thymoma, thyroid carcinoma, uterine carcinosarcoma, uterine corpus endometrial carcinoma, or uveal melanoma or any combination thereof. In some embodiments, the predictive model comprises a machine learning model. In some embodiments, the machine learning model is a regularized machine learning model. In some embodiments, the machine learning model is a combination of one or more machine learning models. In some embodiments, the predictive model identifies and removes said first or second one or more subjects' one or more microbial or non-microbial nucleic acids classified as noise while selectively retaining other said one or more microbial or non-microbial features termed signal. In some embodiments, the first or second set of one or more subjects are non-human mammal. In some embodiments, the first or second set of one or more subjects are human. In some embodiments, the one or more biological samples are liquid biopsies. In some embodiments, the one or more biological samples is whole blood, plasma, serum, saliva, sputum, urine, cerebral spinal fluid, sweat, tears, exhaled breath condensate, stool or any combination thereof. In some embodiments, the first or second set of one or more subjects' treatment outcome comprise efficacy, failure, safety, adverse side effects, or any combination thereof. In some embodiments, the method further comprising concentrating said first or second set of one or more subjects' one or more microbial and non-microbial nucleic acid compositions of said first or second set of subjects' one or more biological samples.

[0006] Another example of the disclosure described herein, in some embodiments, comprises a method of generating a predictive model, comprising: (a) receiving: (i) one or

one or more microbial or non-microbial nucleic acid compositions comprise one or more single nucleotide polymorphisms (SNPs), insertions and/or deletions (INDELS), genomic amplifications and rearrangements or any combination thereof. In some embodiments, the one or more non-microbial nucleic acid compositions comprise cell-free tumor DNA, cell-free tumor RNA, exosome-derived tumor DNA, exosome-derived tumor RNA, circulating tumor cell derived DNA, circulating tumor cell derived RNA, methylation patterns of cell-free tumor DNA, methylation patterns of cell-free tumor RNA, methylation patterns of circulating tumor cell derived DNA and/or methylation patterns of circulating tumor cell derived RNA or any combination thereof. In some embodiments, receiving further comprises said one or more subjects' non-genomic data comprising gender, age, weight, body mass index, dietary factors, cardiovascular function, gastrointestinal function, immunological function, liver function, renal function, albumin concentration, alcohol intake, tobacco or marijuana use, pregnancy, lactation, exercise, comorbidities, occupational exposures, psychological status, other medications, or any combination thereof. In some embodiments, the predictive model is a machine learning model. In some embodiments, the predictive model is a regularized machine learning model. In some embodiments, the predictive model is a combination of one or more machine learning models. In some embodiments, the predictive model identifies and removes said one or more subjects' one or more microbial nucleic acid compositions classified as noise while selectively retaining other said one or more microbial features termed signal. In some embodiments, the one or more subjects are non-human mammal. In some embodiments, the one or more subjects are human. In some embodiments, the one or more liquid biopsies comprise whole blood, plasma, serum, saliva, sputum, urine, cerebral spinal fluid, sweat, tears, exhaled breath condensate, stool, or any combination thereof. In some embodiments, the method further comprises determining a correlation between said one or more subjects' said at least one therapeutic outcome and said one or more sequences of said one or more microbial or non-microbial nucleic acid compositions.

[0007] Another example of the disclosure described herein, in some embodiments, comprises a computer-implemented method for utilizing a predictive model to provide a therapeutic treatment prediction for one or more subjects, the method comprising: (a) receiving a first set of one or more subjects' one or more liquid biopsies comprising one or more non-microbial and microbial nucleic acid compositions genetic sequences and corresponding at least one therapeutic outcome of said first set of one or more subjects' when exposed to a treatment;(b) training a predictive model with said genetic sequences and said

compound for a given subject based on their one or more microbial nucleic acid compositions of DNA or RNA.

[0009] Examples disclosed herein provide a method for a clinical study data analysis system, comprising: (a) receiving (i) a liquid biopsy comprising one or more microbial nucleic acid compositions; and (ii) at least one therapeutic outcome from one or more subjects undergoing treatment in a clinical trial; and (b) analyzing the sequence of the one or more microbial nucleic acid compositions of the one or more subjects; (c) determining a correlation between the one or more subjects' at least one therapeutic outcome and the sequence of the one or more microbial nucleic acid compositions; and (d) generating a predictive model with the correlation where the predictive model provides at least one therapeutic outcome of the one or more microbial nucleic acid compositions of the one or more subjects. In some embodiments, receiving further comprises non-genomic data comprising one or more subjects' gender, age, weight, body mass index, dietary factors, cardiovascular function, gastrointestinal function, immunological function, liver function, renal function, albumin concentration, alcohol intake, tobacco or marijuana use, pregnancy, lactation, exercise, comorbidities, occupational exposures, psychological status, other medications or any combination thereof. In some embodiments, at least one therapeutic outcome comprises therapeutic efficacy, therapeutic failure, therapeutic safety, therapeutic adverse side effect or any combination thereof. In some embodiments, the one or more microbial nucleic acid compositions comprise cell-free (cf) nucleic acids. In some embodiments, the one or more microbial nucleic acid compositions comprise microbial cell-free microbial DNA (cfDNA), cell-free microbial RNA (cfRNA) or any combination thereof. In some embodiments, the one or more microbial nucleic acid compositions comprise an origin of viral, bacterial, archaeal, fungal or any combination thereof. In some embodiments, the treatment is for cancer. In some embodiments, the predictive model is used to analyze the therapeutic outcome of subjects treated for acute myeloid leukemia, adrenocortical carcinoma, bladder urothelial carcinoma, brain lower grade glioma, breast invasive carcinoma, cervical squamous cell carcinoma and endocervical adenocarcinoma, cholangiocarcinoma, colon adenocarcinoma, esophageal carcinoma, glioblastoma multiforme, head and neck squamous cell carcinoma, kidney chromophobe, kidney renal clear cell carcinoma, kidney renal papillary cell carcinoma, liver hepatocellular carcinoma, lung adenocarcinoma, lung squamous cell carcinoma, lymphoid neoplasm diffuse large B-cell lymphoma, mesothelioma, ovarian serous cystadenocarcinoma, pancreatic adenocarcinoma, pheochromocytoma and paraganglioma, prostate adenocarcinoma, rectum adenocarcinoma,

sarcoma, skin cutaneous melanoma, stomach adenocarcinoma, testicular germ cell tumors, thymoma, thyroid carcinoma, uterine carcinosarcoma, uterine corpus endometrial carcinoma, uveal melanoma or any combination thereof. In some embodiments, the predictive model comprises an artificial intelligence machine learning model where the artificial intelligence machine learning model is trained with the one or more microbial nucleic acid compositions of the one or more subjects and the correlation between the one or more subjects' one or more microbial nucleic acid compositions and at least one therapeutic outcome. In some embodiments, the predictive model of at least one therapeutic outcome of the one or more subject is used to triage therapeutic clinical trial subjects into responder, non-responder, non-adverse, and adverse groups prior to therapeutic intervention. In some embodiments, the predictive model is used retrospectively. In some embodiments, the at least one therapeutic outcome of the predictive model is utilized to longitudinally model the course of one or more cancers' response to therapy. In some embodiments, the one or more microbial nucleic acid compositions comprise non-microbial nucleic acid composition comprising one or more single nucleotide polymorphisms (SNPs), insertions and/or deletions (INDELS), genomic amplifications and rearrangements or any combination thereof. In some embodiments, the one or more microbial nucleic acid compositions comprise cell-free tumor DNA, cell-free tumor RNA, exosome-derived tumor DNA, exosome-derived tumor RNA, circulating tumor cell derived DNA, circulating tumor cell derived RNA, methylation patterns of cell-free tumor DNA, methylation patterns of cell-free tumor RNA, methylation patterns of circulating tumor cell derived DNA and/or methylation patterns of circulating tumor cell derived RNA or any combination thereof. In some embodiments, the predictive model is a machine learning model. In some embodiments, the predictive model is a regularized machine learning model. In some embodiments, the predictive model is a combination of one or more machine learning models. In some embodiments, the predictive model identifies and removes the one or more microbial nucleic acid compositions classified as noise while selectively retaining other one or more microbial features termed signal. In some embodiments, the one or more subjects are non-human mammal. In some embodiments, the one or more subjects are human. In some embodiments, the liquid biopsy comprises whole blood, plasma, serum, saliva, sputum, urine, cerebral spinal fluid, sweat, tears, exhaled breath condensate, stool or any combination thereof.

Examples disclosed herein provide a method for a therapeutic treatment study data analysis system, comprising: (a) providing one or more biological samples of one or more subjects wherein a therapeutic treatment outcome of efficacy is demonstrated; (b) providing

thymoma, thyroid carcinoma, uterine carcinosarcoma, uterine corpus endometrial carcinoma, uveal melanoma or any combination thereof. In some embodiments, the artificial intelligence is a machine learning model. In some embodiments, the artificial intelligence is a regularized machine learning model. In some embodiments, the artificial intelligence is a combination of one or more machine learning models. In some embodiments, the treatment outcome predictive model identifies and removes one or more microbial nucleic acids classified as noise while selectively retaining other one or more microbial features termed signal. In some embodiments, the one or more subjects are non-human mammal. In some embodiments, the one or more subjects are human. In some embodiments, the one or more biological samples is a liquid biopsy. In some embodiments, the one or more biological samples is whole blood, plasma, serum, saliva, sputum, urine, cerebral spinal fluid, sweat, tears, exhaled breath condensate, stool or any combination thereof.

[0010] Examples disclosed herein provide a method for a therapeutic treatment study data analysis system, comprising: (a) providing one or more biological samples of one or more subjects wherein a therapeutic treatment outcome of efficacy is demonstrated; (b) providing one or more biological samples of one or more subjects wherein a therapeutic treatment outcome of failure is demonstrated; (c) providing one or more biological samples of one or more subjects wherein a therapeutic treatment outcome of safety is demonstrated; (d) providing one or more biological samples of one or more subjects wherein a therapeutic treatment outcome of adverse side effects is demonstrated; (e) concentrating one or more microbial nucleic acid composition of said one or more subjects' one or more biological sample; (f) analyzing said one or more microbial nucleic acid compositions of said one or more subjects; (g) analyzing said one or more non-microbial nucleic acid compositions of said one or more subjects; (h) receiving one or more non-genomic data of said one or more subjects; (i) training an artificial intelligence wherein a training set comprises one or more microbial nucleic acid compositions, one or more non-microbial nucleic acid compositions, one or more non-genomic data and the therapeutic treatment outcome of one or more subjects; (j) generating a treatment outcome predictive model outcome with said trained artificial intelligence. In some embodiments, the method for a therapeutic treatment study data analysis system further comprises predicting the treatment outcome of an unknown subject with the trained artificial intelligence. In some embodiments, the one or more subjects are non-human mammal. In some embodiments, the one or more biological samples is a liquid biopsy. In some embodiments, the one or more biological samples is whole blood plasma, serum, saliva, sputum, urine, cerebral spinal fluid, sweat, tears, exhaled breath

CLAIMS

What is claimed:

1. A method for generating a therapeutic treatment prediction of one or more subjects, comprising:
    (a) receiving:
        i. one or more liquid biopsies of one or more subjects, wherein said one or more liquid biopsies comprise one or more microbial and non-microbial nucleic acid compositions;
        ii. at least one therapeutic treatment of said one or more subjects; and
        iii. clinical metadata from said one or more subjects;
    (b) determining one or more sequences of said one or more microbial and non-microbial nucleic acid compositions of said one or more subjects; and
    (c) processing said one or more microbial and non-microbial nucleic acid compositions and said clinical metadata with a trained predictive model thereby generating said therapeutic treatment prediction of said one or more subjects, wherein said trained predictive model is trained with a plurality of microbial and non-microbial nucleic acid compositions derived from a liquid biopsy sample of subjects with a corresponding therapeutic outcome and clinical metadata from said subjects.

2. The method of claim 1, wherein said one or more subjects' said at least one therapeutic outcome comprises therapeutic efficacy, therapeutic failure, therapeutic safety, therapeutic adverse side effect or any combination thereof.

3. The method of claim 1, wherein said one or more subjects' one or more microbial nucleic acid compositions comprise cell-free nucleic acids.

4. The method of claim 1, wherein said one or more subjects' one or more microbial nucleic acid compositions comprise microbial cell-free microbial DNA, cell-free microbial RNA or any combination thereof.

5. The method of claim 1, wherein said one or more subjects' one or more microbial nucleic acid compositions comprise an origin of viral, bacterial, archaeal, fungal sources or any combination thereof.

6. The method of claim 1, wherein said therapeutic treatment treats cancer.

7. The method of claim 1, wherein said predictive model is used to analyze a therapeutic outcome of subjects treated for acute myeloid leukemia, adrenocortical carcinoma, bladder urothelial carcinoma, brain lower grade glioma, breast invasive carcinoma, cervical squamous cell carcinoma and endocervical adenocarcinoma, cholangiocarcinoma, colon adenocarcinoma, esophageal carcinoma, glioblastoma multiforme, head and neck squamous cell carcinoma, kidney chromophobe, kidney renal clear cell carcinoma, kidney renal papillary cell carcinoma, liver hepatocellular carcinoma, lung adenocarcinoma, lung squamous cell carcinoma, lymphoid neoplasm diffuse large B-cell lymphoma, mesothelioma, ovarian serous cystadenocarcinoma, pancreatic adenocarcinoma, pheochromocytoma and paraganglioma, prostate adenocarcinoma, rectum adenocarcinoma, sarcoma, skin cutaneous melanoma, stomach adenocarcinoma, testicular germ cell tumors, thymoma, thyroid carcinoma, uterine carcinosarcoma, uterine corpus endometrial carcinoma, or uveal melanoma or any combination thereof.

8. The method of claim 1, wherein said predictive model comprises an artificial intelligence machine learning model, wherein said artificial intelligence machine learning model is trained with said one or more microbial and non-microbial nucleic acid composition said one or more sequences of said one or more subjects and said correlation between said one or more subjects' said one or more microbial and non-microbial nucleic acid composition said one or more sequences and said at least one therapeutic outcome.

9. The method of claim 1, wherein said therapeutic outcome of said one or more subjects is used to triage therapeutic clinical trial subjects into responder, non-responder, non-adverse, and adverse groups prior to therapeutic intervention.

10. The method of claim 1, wherein said trained predictive model is used retrospectively.

11. The method of claim 1, wherein said one or more subjects' said at least one therapeutic outcome of said trained predictive model is utilized to longitudinally model the course of one or more cancers' response to therapy.

12. The method of claim 1, wherein said one or more subjects' one or more microbial or non-microbial nucleic acid compositions comprise one or more single nucleotide polymorphisms, insertions, deletions, genomic amplifications, rearrangements, or any combination thereof.

13. The method of claim 1, wherein said one or more subjects' one or more non-microbial nucleic acid compositions comprise cell-free tumor DNA, cell-free tumor RNA, exosome-derived tumor DNA, exosome-derived tumor RNA, circulating tumor cell derived DNA, circulating tumor cell derived RNA, methylation patterns of cell-free tumor DNA, methylation patterns of cell-free tumor RNA, methylation patterns of circulating tumor cell derived DNA and/or methylation patterns of circulating tumor cell derived RNA, or any combination thereof.

14. The method of claim 1, further comprising receiving said one or more subjects' non-genomic data comprising gender, age, weight, body mass index, dietary factors, cardiovascular function, gastrointestinal function, immunological function, liver function, renal function, albumin concentration, alcohol intake, tobacco or marijuana use, pregnancy, lactation, exercise, comorbidities, occupational exposures, psychological status, other medications, or any combination thereof.

15. The method of claim 1, wherein said predictive model is a machine learning model, a regularized machine learning model, or a combination thereof.

16. The method of claim 1, wherein said predictive model is a combination of one or more machine learning models.

17. The method of claim 1, wherein said predictive model identifies and removes said one or more subjects' one or more microbial or non-microbial nucleic acid compositions classified as noise while selectively retaining other one or more microbial or non-microbial features termed signal.

18. The method of claim 1, further comprising determining taxonomic assignments from said one or more sequences of said one or more microbial nucleic acid compositions.

19. The method of claim 1, wherein said one or more subjects are human or non-human mammals.

20. The method of claim 1, wherein said liquid biopsy comprises whole blood, plasma, serum, saliva, sputum, urine, cerebral spinal fluid, sweat, tears, exhaled breath condensate, stool, or any combination thereof.