

TITLE

GENETIC ANALYSIS

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims the priority of U.S. Provisional Application Ser. No. 61/277,394, filed September 23, 2009, the entire disclosure of which is incorporated herein by reference.

BACKGROUND

Field of the Invention

[0002] The present invention generally relates to biology and genetics. More specifically, the invention relates to methods and compositions for genetic analysis of an organism.

Description of the Related Art

[0003] The genomes of organisms contain a vast amount of information that can be mined in order to predict, identify, or describe phenotypes of an organism, such as diseases, conditions, disorders, traits, characteristics, morphology, biochemical properties, or physiologic properties. Phenotypes can also be affected, determined, or predicted from non-genetic factors, or from some combination of genetic and non-genetic factors. There is an unmet need for an intelligent approach to using genetic and non-genetic information to predict, identify, analyze or describe phenotypes in an organism.

SUMMARY OF THE INVENTION

[0004] A first aspect provided herein is a method of determining an organ system score of an organism comprising: identifying a set of genetic variants in an organism, wherein said genetic variants relate to an organ system phenotype; calculating the predisposition or carrier status of said organism for at least two phenotypes wherein said predisposition or carrier status is based on said set of genetic variants; combining the results of the previous step to obtain an organ system score; and, reporting said organ system score to said organism, a health care provider of said organism, or a third party. For example, reporting an organ system score may comprise reporting to an organism's veterinarian, a herder, a rancher, a company that owns the organism, an individual who owns the organism, and/or an organism's caretaker.

[0005] A second aspect provided herein is a method of determining an overall genetic health score of an organism comprising: identifying a set of genetic variants in an organism; calculating two or more organ system scores according to the first 3 steps of the first aspect; combining said two or more organ system scores to obtain an overall genetic health score; and, reporting said overall genetic health score in a report to said organism, a health care provider of said organism, or third party. For instance, reporting an overall genetic health score may comprise reporting to an organism's

veterinarian, a herder, a rancher, a company that owns the organism, an individual who owns the organism, and/or an organism's caretaker.

[0006] In an embodiment of the methods of the first two aspects, said organ system is selected from the group consisting of: cardiovascular; heart; lung; dermatology; development and learning; ear, nose, and throat; dental; endocrinology; pancreas; thyroid; gastroenterology; hepatology; liver; gall bladder; gynecology; hematology and oncology; immunology; allergy; lactation system, central nervous system, psychological system including but not limited to temperament, infectious diseases; men's health; metabolic diseases; rare diseases; male health; musculoskeletal; neonatology; neurology; obstetrics; ophthalmology; pharmacology, toxicology; anesthesiology; psychiatry; reproductive health, rheumatology; sexuality; fertility; sleep medicine; surgery; syndromes; temperament, laryngology; traits and special abilities; obstetrics, otology; urology and nephrology; and vascular; geriatric health; and female health.

[0007] In some embodiments of the methods of the first two aspects, said organ system score in said report is divided into two or more specific phenotypes. In other embodiments of the methods provided at least one of said phenotypes is a rare disease. In further embodiments of the methods provided, at least one of said phenotypes follows monogenic inheritance. In another embodiment of the methods provided, at least one of said phenotypes follows multifactorial or polygenic inheritance. In yet another embodiment of the methods provided, at least one of said phenotypes follows monogenic inheritance; and at least one of said phenotypes follows multifactorial or polygenic inheritance.

[0008] In an embodiment of the methods of the first two aspects, said reporting is by e-mail, a website, paper, a telephone call, on a CD-ROM, on an electronic storage device, a text message, or in person. In an embodiment of the methods of the first two aspects, said reporting is by transmission over a network. In some embodiments of the methods of the first two aspects, the methods further comprise providing a pedigree analysis of said organism to said organism's owner, organism's potential owner, organism's caretaker, a veterinarian or other healthcare provider of said organism, a herder, a rancher, a government agency, an entity, or third party. In some embodiments of the methods of the first two aspects, the methods further comprise providing a medical recommendation based on said score by a veterinarian, biologist, physician, or other qualified person to said organism's owner, organism's potential owner, organism's caretaker, a veterinarian or other healthcare provider of said organism, a government agency, an entity, or third party. In other embodiments, said veterinarian is a generalist. In further embodiments, said veterinarian, biologist, breeder, specialist in the field, or researcher is selected from the group consisting of: artificial insemination specialist, anesthesiologist, bacteriologist, cattle specialist, cat specialist, cardiologist, chicken specialist, cloning specialist, dermatologist, dog specialist, endocrinologist, gastroenterologist, geneticist, goat specialist, governmental agency representative, cultivator, hematologist, horse specialist, infectious disease specialist, immunologist, fertility specialist, mouse specialist, nutrition and obesity specialist, neurologist, obstetrician, gynecologist, oncologist, ophthalmologist, pig specialist, pharmacologist,

primate specialist, psychiatrist, pulmonologist, rancher, rat specialist, reproduction specialist, rheumatologist, surgeon, transgenic specialist, urologist, virologist.

[0009] In some embodiments of the methods of the first two aspects, said set of genetic variants comprises genetic variants for at least five genes. In other embodiments of the methods of the first two aspects, said set of genetic variants comprises at least two genetic variants, each of which is correlated to the same phenotype. In some embodiments of the methods of the first two aspects, said set of genetic variants comprises at least 10 single nucleotide polymorphisms. In some embodiments of the methods of the first two aspects, said set of genetic variants comprises at least 50 single nucleotide polymorphisms, wherein each SNP is correlated to a phenotype. In some embodiments of the methods of the first two aspects, said set of genetic variants comprises at least one SNP sequence not listed in a public database, wherein said at least one SNP sequence is correlated to a phenotype.

[0010] In some embodiments of the methods of the first two aspects, calculating of said score includes the gender, breed, strain, age, weight, purpose of organism (including but not limited to companion to humans, work-related, production-related, transgenic related, food-related, environment-related, aesthetic-related), where organism will be born and live (including but not limited to a country farm, a city farm, a farm with less than 100 animals, a farm with more than 100 animals, a farm with more than 1,000 animals, a farm with more than 10,000 animals, an urban household with children, an urban household without children, a fishery, a stable, a mill, a ranch, a field, a greenhouse, a valley, a mountain, and/or free-range). In some embodiments of the methods of the first two aspects, said reporting is performed within one week of the first step. In some embodiments of the methods of the first two aspects, said reporting is performed only when a decreased predisposition for said phenotype is determined. In some embodiments of the methods of the first two aspects, said reporting is performed only when an increased predisposition for said phenotype is determined. In some embodiments of the methods of the first two aspects, said at least two phenotypes are selected.

[0011] In some embodiments of the methods of the first two aspects, said calculating is performed by consulting a database comprising at least one scientific article about a study that shows a correlation or association between at least one genetic variant and at least one phenotype. In an embodiment of the methods, said scientific article is ranked against other scientific articles based on one or more of the following factors: the number of organisms in the phenotype cohort of said study, the number of organisms in control cohort of said study, the total number of organisms in said study, the caliber of the institution that conducted said study, the place said study was conducted, the year said study was published, the reputation of any of the authors of said study, and the rating of the journal where said scientific article appeared. In some embodiments of the methods, rating of said journal is based on one or more of the following factors: the Impact Factor of said journal, the Immediacy Index of said journal, the cited half-life of said journal, and the Page Rank of said journal.

[0012] In further embodiments of the methods of the first two aspects, calculating is performed by consulting a database comprising a ranking system that rates genetic variants based on the relative strength of the data reported from studies. In another embodiment, calculating excludes a genetic variant in linkage disequilibrium with a genetic variant with a higher rating as determined by said ranking system. In other embodiments, said ranking system is based on one or more of the following factors: the number of studies reporting a correlation or association between said at least one genetic variant and said at least one phenotype; the number of studies showing contradictory results regarding said correlation or association; the aggregate number of organisms included in said studies; the type of study conducted; the degree to which the study has been replicated; and the year the study was conducted.

[0013] In some embodiments of the methods of the first two aspects, said calculating is performed by consulting a database comprising a ranking system that rates genetic variants based on the relative clinical value of the association between the genetic variant and the phenotype. In an embodiment, relative clinical value is determined by one or more medical specialists. In some embodiments, relative clinical value is determined by one or more: veterinarian, biologist, breeder, specialist in the field, or researcher is selected from the group consisting of: artificial insemination specialist, anesthesiologist, bacteriologist, cattle specialist, cat specialist, cardiologist, chicken specialist, cloning specialist, dermatologist, dog specialist, endocrinologist, gastroenterologist, geneticist, goat specialist, cultivator, hematologist, horse specialist, infectious disease specialist, immunologist, fertility specialist, mouse specialist, nutrition and obesity specialist, neurologist, obstetrician, gynecologist, oncologist, ophthalmologist, pig specialist, pharmacologist, primate specialist, psychiatrist, pulmonologist, rancher, rat specialist, reproduction specialist, rheumatologist, surgeon, transgenic specialist, urologist, virologist. In some embodiments of the methods of the first two aspects, said methods are performed at a ranch, farm, veterinarian's office, in the field, in the wild, at the owner's home, at a government facility, at a supermarket, at a food testing facility, at a corporation. In some embodiments of the methods of the first two aspects, said set of genetic variants is generated using at least one panel from FIGS. 15-20.

[0014] A third aspect provided herein is a method of determining and reporting the predisposition or carrier status of an organism for a reflex phenotype comprising: a) identifying a set of genetic variants in an organism, wherein each of said genetic variants is correlated with a phenotype; b) determining the predisposition or carrier status of said organism to an initial phenotype and to a reflex phenotype, wherein said predisposition or carrier status is based on said set of genetic variants; and c) reporting said predisposition or carrier status to said organism, to a owner, veterinarian, biologist, breeder, specialist in the field, or researcher, government agencies, of or in-charge of said organism, or to a third party, wherein the reporting of the predisposition or carrier status to the reflex phenotype depends on the outcome of said determination of predisposition or carrier status to the first phenotype.

[0015] In an embodiment, said reflex phenotype is reported when said organism is predisposed to, at risk of, or a carrier of said initial phenotype and/or has already been known to have said initial phenotype. In some embodiments, said reflex phenotype is reported when said organism is not predisposed to, at risk of, or a carrier of said initial phenotype. In some embodiments, said reflex phenotype is reported concurrently with said initial phenotype. In other embodiments, said reflex phenotype is reported subsequently to said initial phenotype. In further embodiments, said reflex phenotype is not reported when said organism is not predisposed to, at risk of, or a carrier of said initial phenotype. In another embodiment, said reflex phenotype is a phenotype that is not the initial phenotype.

[0016] In an embodiment, said determining of the predisposition or carrier status of the organism to said reflex phenotype is determined subsequently to the determining of the predisposition or carrier status of the organism for said initial phenotype. In some embodiments, said reflex phenotype is a disease that is positively correlated with said initial phenotype. In some embodiments, said initial phenotype is a disease and said reflex phenotype is a symptom or sequela of said disease. In some embodiments, said reflex phenotype is a trait that is positively correlated with said initial phenotype. In some embodiments, said initial phenotype is a trait and said reflex phenotype is a symptom or sequela of said trait. In other embodiments, said initial phenotype is a disease or disorder and said reflex phenotype is a side effect of, or response to, a treatment for said initial phenotype. In other embodiments, said predisposition or carrier status is determined from at least two genetic variants. In further embodiments, at least two genetic variants are correlated with the same phenotype.

[0017] A fourth aspect provided is a method of predicting a genetic predisposition or carrier status of a potential offspring comprising: a) identifying one or more genetic variants in the genome of the potential mother of a potential offspring, or obtaining one or more previously-identified genetic variants in the genome of the potential mother, wherein each of the genetic variants is associated with a phenotype; b) identifying one or more genetic variants in the genome of the potential father of a potential offspring, or obtaining one or more previously-identified genetic variants in the genome of the potential father, wherein each of the genetic variants is associated with a phenotype; c) based on the set of genetic variants, calculating the predisposition or carrier status of the potential offspring's mother for the phenotype; d) calculating the predisposition or carrier status of the potential offspring's father for the phenotype wherein the predisposition or carrier status is based on the set of genetic variants; e) calculating the potential offspring's predisposition or carrier status for the phenotype wherein the calculating is based on combining the results of step c) and d); and, optionally, f) repeating steps a) through e), wherein the potential mother is different from the potential mother of step a), or wherein the potential father is different from the potential father of step b). In an embodiment, the predisposition is the highest potential risk. In an embodiment, the predisposition is the lowest potential risk.

[0018] In an embodiment of the fourth aspect, the method further comprises identifying or obtaining the genetic location of the genetic variants of step a) and step b), wherein said genetic location is an autosomal chromosome, a non-autosomal chromosome, a mitochondrial chromosome, a cytoplasmic chromosome, a plasmid chromosome, or a chloroplast chromosome. In some embodiments of the fourth aspect, the method further comprises the steps of adjusting the result of step c) in light of the results obtained in the previous embodiment and adjusting the result of step d) in light of the results obtained in the previous embodiment. In other embodiments of the fourth aspect, said identifying is by nucleic acid array or sequencing apparatus. Certain embodiments of the fourth aspect, comprise reporting a predicted genetic predisposition or carrier status of a potential offspring in a report to a company that owns the potential mother or father, an individual who owns the potential mother or father, a company or individual that would own the potential offspring or a third party. For instance, reporting may comprise reporting to a veterinarian, a herder, a rancher or a caretaker.

[0019] In further embodiments of the fourth aspect, the potential mother in step f) is the same as the potential mother in step a) and the potential father in step f) is different from the potential father in step b) and the method further comprising the step of comparing the result from step e) with the result from step f). In a specific embodiment, the method further comprises the step of identifying the potential father of a potential offspring with the highest risk or predisposition for a phenotype and/or the lowest risk or predisposition for a phenotype. In a further embodiment of the fourth aspect, steps a) through e) are repeated with a plurality of potential mothers and/or a plurality of potential fathers and the results are combined to predict the probability of a genetic predisposition or carrier status of a potential offspring from a population of potential mothers and/or fathers. For example, the plurality of potential mothers and/or father may constitute a breeding population, such as a herd, and repeating analysis with a plurality of potential mother and/or fathers can be used to predict a predisposition or carrier status of a potential offspring from the breeding population or to select potential mother and/or fathers from the population to be used for breeding.

[0020] In yet further embodiments of the fourth aspect, the potential father in step f) is the same as the potential father in step b) and the potential mother in step f) is different from the potential mother in step a) and the method further comprising the step of comparing the result from step e) with the result from step f). In an embodiment of the fourth aspect, the method further comprises the step of repeating step f) one or more times. In a specific embodiment, the method further comprises the step of identifying the potential mother of a potential offspring with the highest risk or predisposition for a phenotype and/or the lowest risk or predisposition for a phenotype.

[0021] In some embodiments of the fourth aspect, the potential mother in step a) and the potential father in step b) are both members of the same species. In other embodiments of the fourth aspect, the potential mother in step a) and the potential father in step b) are both cows. In another embodiment of the fourth aspect, the potential mother in step a) and the potential father in step b) are both cattle. In another embodiment of the fourth aspect, the potential mother in step a) and the potential father in

step b) are both cats. In another embodiment of the fourth aspect, the potential mother in step a) and the potential father in step b) are both mice. In another embodiment of the fourth aspect, the potential mother in step a) and the potential father in step b) are both rats. In other embodiments of the fourth aspect, the potential mother in step a) and the potential father in step b) are both horses. In further embodiments of the fourth aspect, the potential mother in step a) and the potential father in step b) are both pigs. In another embodiment of the fourth aspect, the potential mother in step a) and the potential father in step b) are both dogs. In another embodiment of the fourth aspect, the potential mother in step a) and the potential father in step b) are both cats. In another embodiment of the fourth aspect, the potential mother in step a) and the potential father in step b) are both chickens. In another embodiment of the fourth aspect, the potential mother in step a) and the potential father in step b) are both primates. In another embodiment of the fourth aspect, the potential mother in step a) and the potential father in step b) are both goats. In another embodiment of the fourth aspect, the potential mother in step a) and the potential father in step b) are both turkeys. In yet another embodiment of the fourth aspect, the potential mother in step a) and the potential father in step b) are both sheep. In some embodiments of the fourth aspect, the potential mother in step a) and the potential father in step b) are both mammals. In other embodiments of the fourth aspect, the potential mother in step a) and the potential father in step b) are both plants. In other embodiments of the fourth aspect, the potential mother in step a) and the potential father in step b) are both fish. In another embodiment of the fourth aspect, the potential mother in step a) and the potential father in step b) are members of different species.

[0022] In an embodiment of the fourth aspect wherein the method further comprises identifying or obtaining the genetic location of the genetic variants of step a) and step b), wherein said genetic location is an autosomal chromosome, a non-autosomal chromosome, or mitochondrial chromosome, a cytoplasmic chromosome, a plasmid chromosome, or a chloroplast chromosome the method also further comprises the step of identifying the potential father of a potential offspring with the highest risk or predisposition for a phenotype.

[0023] A fifth aspect provided herein is an array comprising at least 25 oligonucleotide sequences attached to a support, wherein each of said sequences is associated with a genetic variant, and the majority of said genetic variants are linked to at least one citation for a scientific article correlating said genetic variant to a phenotype. In an embodiment of the array, each of said genetic variants is correlated to a phenotype.

[0024] A sixth aspect provided herein is an array comprising at least 25 oligonucleotide sequences attached to a support, wherein at least 5% of said sequences are not listed in a public database, and each of said sequences is associated with a genetic variant correlated to a phenotype.

[0025] A seventh aspect provided herein is an array comprising at least 25 oligonucleotide sequences attached to a support, wherein each of said sequence is used to determine an organ system score for an organism. In an embodiment, of the array, said organ system is selected from the group consisting of:

cardiovascular; heart; lung; dermatology; development and learning; ear, nose, and throat; dental; endocrinology; pancreas; thyroid; gastroenterology; hepatology; liver; gall bladder; gynecology; hematology and oncology; immunology; immunology and allergy; infectious diseases; men's health; metabolic diseases; rare diseases; male health; musculoskeletal; neonatology; neurology; obstetrics; ophthalmology; pharmacology, toxicology; anesthesiology; psychiatry; reproductive health; rheumatology; sexuality; fertility; sleep medicine; surgery; syndromes; temperament, laryngology; traits and special abilities; otology; urology and nephrology; and vascular; geriatric health; and female health.

[0026] An eighth aspect provided herein is an array comprising at least 25 oligonucleotide sequences attached to a support, wherein each of said sequences is linked to at least one recommendation by a veterinarian, trainer, rancher, herder, scientist, biologist, physician, or other qualified person, owner, caretaker, other healthcare provider of said organism, a government agency, specialist, or third party. In some embodiments of the array, said specialist is selected from the group consisting of: artificial insemination specialist, anesthesiologist, bacteriologist, cattle specialist, cat specialist, cardiologist, chicken specialist, cloning specialist, dermatologist, dog specialist, endocrinologist, gastroenterologist, geneticist, goat specialist, governmental agency representative, cultivator, hematologist, horse specialist, infectious disease specialist, immunologist, fertility specialist, mouse specialist, nutrition and obesity specialist, neurologist, obstetrician, gynecologist, oncologist, ophthalmologist, pig specialist, pharmacologist, primate specialist, psychiatrist, pulmonologist, rancher, rat specialist, reproduction specialist, rheumatologist, surgeon, transgenic specialist, urologist, virologist.

[0027] A ninth aspect provided herein is a system comprising: a database comprising at least 25 oligonucleotide sequences attached to a support, wherein each of said sequences are associated with a genetic variant; code for linking each of said sequences to at least one recommendation by a veterinarian, biologist, physician, or other qualified person, owner, caretaker, other healthcare provider of said organism, a government agency, specialist, or third party; and, code for generating a report comprising said recommendation.

[0028] A tenth aspect provided herein is a system comprising: a database comprising at least 25 oligonucleotide sequences attached to a support, wherein each of said sequences are associated with a genetic variant; code for calculating one or more organ system scores based on said sequences; and, code for generating a report comprising said score.

[0029] In some embodiments of the ninth and tenth aspects is a system further comprising: code linking each of said sequences to at least one citation for a scientific article correlating said genetic variant to a phenotype or trait. In some embodiments of the ninth and tenth aspects is a system, each of said genetic variants is correlated to a phenotype. In other embodiments, at least one of said phenotypes is a rare disease. In further embodiments, at least one of said phenotypes is a monogenic phenotype. In another embodiment, at least one of said phenotypes is a multifactorial phenotype.

[0030] In some embodiments of the ninth aspects said specialist is selected from the group consisting of: artificial insemination specialist, anesthesiologist, bacteriologist, cattle specialist, cat specialist, cardiologist, chicken specialist, cloning specialist, dermatologist, dog specialist, endocrinologist, gastroenterologist, geneticist, goat specialist, governmental agency representative, cultivator, hematologist, horse specialist, infectious disease specialist, immunologist, fertility specialist, mouse specialist, nutrition and obesity specialist, neurologist, obstetrician, gynecologist, oncologist, ophthalmologist, pig specialist, pharmacologist, primate specialist, psychiatrist, pulmonologist, rancher, rat specialist, reproduction specialist, rheumatologist, surgeon, transgenic specialist, urologist, virologist..

[0031] In some embodiments of the ninth aspects said organ system is selected from the group consisting of: cardiovascular; heart; lung; dermatology; development and learning; ear, nose, and throat; dental; endocrinology; pancreas; thyroid; gastroenterology; hepatology; liver; gall bladder; gynecology; hematology and oncology; immunology; immunology and allergy; infectious diseases; men's health; metabolic diseases; rare diseases; male health; musculoskeletal; neonatology; neurology; obstetrics; ophthalmology; pharmacology, toxicology; anesthesiology; psychiatry; reproductive health, rheumatology; sexuality; fertility; sleep medicine; surgery; syndromes; temperament, laryngology; traits and special abilities; otology; urology and nephrology; and vascular; geriatric health; and female health.

[0032] An eleventh aspect provided herein is a computer readable medium, comprising a set of instructions to cause a computer to perform the steps of comparing input data comprising genetic variant information from an organism's genome against a set of data comprising association data correlating genetic variants with phenotypes and generating an output comprising an evaluation of the predisposition, or carrier status, of said organism for at least two phenotypes.

[0033] A twelfth aspect provided herein is a computer program product comprising a computer readable medium having computer program logic recorded therein for enabling a processor to determine the genetic predisposition or carrier status of an organism, said computer logic comprising: a) a storing procedure that enables the processor to store a set of information comprising a set of correlations, wherein each correlation comprises a correlation between a genetic variant and a phenotype; b) a receiving procedure that enables the processor to receive a set of information comprising one or more genetic variants within the genome of a subject; c) a comparing procedure to compare input data from the genome of said subject against the set of information in step a); d) a calculating procedure to calculate one or more scores based on said genetic variants within the genome of said subject; and e) an output procedure to provide a report of said comparison.

[0034] In some embodiments of the computer program product of the eleventh and twelfth aspects, the computer program product further comprising: a linking procedure linking each of said genetic variants to at least one citation for a scientific article or association study correlating said genetic variant to a phenotype. In some embodiments of the computer program product of the eleventh and

twelfth aspects, at least one of said phenotypes follows monogenic inheritance and at least one of said phenotypes follows multifactorial or polygenic inheritance.

[0035] A thirteenth aspect provided herein is a method of selecting a haploid genome containing cell comprising: applying a sample from said cell to an array; and, determining a set of genetic variants of said cell. In an embodiment, said cell is of male origin. In some embodiments, said cell is of female origin. In some embodiments, said cell is an oocyte. In some embodiments, said cell is a sperm cell. In other embodiments, the method further comprises selecting said haploid genome containing cell to produce a diploid embryo. In further embodiments, the method further comprises incorporating one or more factors chosen from the gender, breed, strain, age, weight, purpose of organism (including but not limited to companion to humans, work-related, production-related, transgenic related, food-related, environment-related, aesthetic-related), where organism will be born and live (including but not limited to a country farm, a city farm, a farm with less than 100 animals, a farm with more than 100 animals, a farm with more than 1,000 animals, a farm with more than 10,000 animals, an urban household with children, an urban household without children, a research facility, in a cage, free range, , in the wild, a fishery, a stable, a mill, a ranch, a field, a greenhouse, a valley, a mountain, and/or free-range), family history of phenotype, and organism history of phenotype of the donor of said haploid genome containing cell.

[0036] A fourteenth aspect provided herein is an array comprising at least one oligonucleotide for detecting a degree of risk to an initial phenotype and a second oligonucleotide for detecting a degree of risk to a reflex phenotype. In an embodiment, said initial phenotype is a disease or disorder and said reflex phenotype is the response to or effectiveness of a drug for treating said disease or disorder, a drug or treatment that modifies a phenotype. In some embodiments, said initial phenotype is cancer and said reflex phenotype is the response to a cancer drug. In some embodiments, said initial phenotype is milk production and said reflex phenotype is the response to a drug that increases milk production. In some embodiments, said initial phenotype is a disease and said reflex phenotype is the response to a drug that prevents or treats said disease. In some embodiments, said initial phenotype is a fertility rate and said reflex phenotype is the response to a drug that increases fertility rates. In some embodiments, said initial phenotype is racing speed and said reflex phenotype is the response to a drug that increases racing speed. In some embodiments, said initial phenotype is temperament and said reflex phenotype is the response to a drug that makes temperament more docile and/or prevents acts of aggression. In some embodiments, said initial phenotype is food allergy and said reflex phenotype is the response to a specific food.

[0037] In some embodiments, the genetic variants are present in nucleic acids provided from the organism as a sample, which sample may have been previously obtained, i.e. prior to performance of the methods provided herein. In some embodiments, the genetic variants are present in an organism's genome or nucleic acids provided by the organism or a third party as a sample, which sample may have been previously obtained, i.e. prior to performance of the methods provided herein.

[0038] One aspect provides a nucleic acid sample from an organism for use in a method of determining the risk, predisposition, or carrier status of that organism for one or more phenotypes, the method comprising: identifying by nucleic acid array or sequencing apparatus one or more genetic variants in an organism or a set of genetic variants in an organism, wherein each of said genetic variants is correlated with a phenotype; using a computer to determine the predisposition of said organism for a phenotype wherein said predisposition is based on said set of genetic variants or said one or more genetic variants; and, optionally, providing a report of said predisposition to said organism.

[0039] Another aspect provided herein is related to gender specific health phenotypes and is a method of determining the predisposition or carrier status of an organism for two or more gender specific health phenotypes comprising: identifying by nucleic acid array, sequencing apparatus, or nanopore sequencer a set of genetic variants in an organism, wherein each of said genetic variants is correlated with a gender-specific health phenotype; using a computer to determine the predisposition or carrier status of said organism for at least two phenotypes, wherein said predisposition or carrier status is based on said set of genetic variants; providing a report of said predisposition or carrier status to said organism, to a health care provider of said organism, or to a third party; and optionally combining the predisposition or carrier status of said organism for said at least two phenotypes into a gender-specific health score, wherein said score is reported to said organism, to a health care provider, or to a third party.

[0040] In an embodiment of the gender specific health aspect, at least two phenotypes comprise an initial phenotype and a reflex phenotype, wherein said reflex phenotype is a phenotype that is not the initial phenotype, and wherein the reporting of the predisposition or carrier status of said organism for the reflex phenotype depends on the outcome of said determination of predisposition or carrier status of said organism for the first phenotype. In some embodiments, at least two phenotypes are at least two phenotypes listed in any of the panels in FIGS. 15-20. In other embodiments, at least two phenotypes comprise at least five phenotypes. In further embodiments, at least two phenotypes comprise: at least one phenotype that follows monogenic inheritance; and at least one phenotype that follows multifactorial or polygenic inheritance. In further embodiments, at least two phenotypes comprise: at least one phenotype that is a trait; and at least one phenotype that is a disease.

[0041] In another embodiment of the gender specific health aspect, at least two phenotypes comprises at least two of the following phenotypes: female fertility, infertility, spontaneous abortion, miscarriages, or reproduction system abnormalities; osteoporosis or osteoporotic fracture; obesity or leanness; heart disease; thrombophilia or thromboembolic disease; cancer of female reproductive organs; skin cancer or sensitivity to ultraviolet light; lung cancer; colorectal cancer; hypertension or blood pressure level; polycystic ovary syndrome; or stroke. In yet another embodiment, at least two phenotypes comprises at least two of the following phenotypes: myocardial infarction; breast cancer; osteoporosis or osteoporotic fracture; Alzheimer's disease; thrombophilia or thromboembolic disease;

cardiac arrhythmia or cardiac conduction abnormality, cardiomyopathy; obesity or leanness; skin cancer or sensitivity to ultraviolet light; or lung cancer.

[0042] In an embodiment of the gender specific health aspect, at least two phenotypes comprises at least two of the following phenotypes: female fertility, infertility, spontaneous abortion or miscarriages; ovulatory defects, premature ovarian failure or ovarian dysgenesis; thrombophilia or thromboembolic disease; fetal viability; bleeding diathesis, coagulation disorders or hemophilia; primary or secondary sex characteristics, sex reversal or hypogonadism; or hypogonadism. In some embodiments, at least two phenotypes comprises at least two of the following phenotypes: breast cancer; thrombophilia or thromboembolic disease; infectious disease susceptibility; ovarian abnormalities or failure; or ovarian cancer.

[0043] In further embodiments, at least two phenotypes comprises at least two of the following phenotypes: male fertility or infertility; heart disease; thrombophilia or thromboembolic disease; cardiac arrhythmia or cardiac conduction abnormality; cardiomyopathy, cancer of male reproductive organs; skin cancer or sensitivity to ultraviolet light; lung cancer; colorectal cancer; hypertension or blood pressure level; or stroke.

[0044] In another embodiment of the gender specific health aspect, at least two phenotypes comprises at least two of the following phenotypes: myocardial infarction; skin cancer; colorectal cancer; prostate cancer; alopecia; thrombophilia or thromboembolic disease; cardiac arrhythmia or cardiomyopathy. In yet another embodiment, at least two phenotypes comprises at least two of the following phenotypes: male fertility or infertility; erectile dysfunction medication treatment, effectiveness or sensitivity; peripheral arterial disease; fetal viability; primary or secondary sex characteristics, sex reversal or hypogonadism; or hypogonadism.

[0045] In an embodiment of the gender specific health aspect, at least two phenotypes comprises at least two of the following phenotypes: male fertility or infertility; erectile dysfunction medication treatment, effectiveness or sensitivity; prostathymia or cardiac conduction abnormality; cancer; nephrolithiasis or urolithiasis; bladder cancer, kidney cancer, or adrenal cancer; IgA nephropathy; diabetic nephropathy; polycystic kidney disease. In some embodiments, at least two phenotypes comprises at least two of the following phenotypes: sexual attraction; pair bonding; personality traits; degree of relationship commitment or divorce potential; or pheromone perception.

[0046] In other embodiments of the gender specific health aspect, said reflex phenotype is reported when said organism has an increased predisposition or carrier status for said initial phenotype. In further embodiments, said reflex phenotype is reported when said organism has a decreased predisposition or carrier status for said initial phenotype. In another embodiment, said reflex phenotype is not reported if the organism has neither a decreased or increased predisposition or carrier status for said initial phenotype. In yet another embodiment, said reflex phenotype is reported concurrently with said initial phenotype. In an embodiment, said reflex phenotype is reported subsequently to said initial phenotype. In some embodiments, the determination of the predisposition

or carrier status of the organism for said reflex phenotype is determined subsequently to the determination of the predisposition or carrier status of the organism for said initial phenotype. In other embodiments, said reflex phenotype is a disease that is positively correlated with said initial phenotype. In further embodiments, said initial phenotype is a disease and said reflex phenotype is a symptom of said disease. In another embodiment, said initial phenotype is a disease or disorder and reflex phenotype is a side effect of, or response to, a treatment for said initial phenotype.

[0047] In yet another embodiment of the gender specific health aspect, said initial phenotype is osteoporosis or osteoporotic fracture, and said reflex phenotype is one or more selected from the group consisting of: effects of specific diets on bone mineral density or osteoporosis; and effect of caffeine consumption on bone mineral density or osteoporosis. In an embodiment, said initial phenotype is obesity or leanness, and said reflex phenotype is one or more selected from the group consisting of: amount of feed needed to gain weight; change in body fat with age or diet; exercise intolerance, or optimal exercise regimen.

[0048] In another embodiment of the gender specific health aspect, said initial phenotype is a trait, and said reflex phenotype is an associated trait or disease.

[0049] In an embodiment of the gender specific health aspect, two or more phenotypes are selected. In some embodiments, said set of genetic variants is identified using a high density DNA microarray. In other embodiments, said set of genetic variants is identified by sequencing genomic DNA from said organism. In further embodiments, said organism is of the female gender. In another embodiment, said organism is of the male gender.

[0050] Another second aspect of gender specific health provided herein is a gender specific health set of probes, wherein said set comprises probes, wherein each of said probes is specifically selected to detect a genetic variant correlated with a gender-specific health phenotype. In some embodiments of the gender-specific health set of probes, said set detects at least two phenotypes listed in FIGS.15-20. In other embodiments, the gender-specific health set of probes, said set comprises at least two probes, and each of said at least two probes detects a different genetic variant, and wherein each of said different genetic variants is correlated to the same phenotype.

[0051] Another aspect provided herein is related to Medical Care phenotypes and is a method of determining the predisposition or carrier status of an organism for two or more Medical Care phenotypes comprising: identifying by nucleic acid array, sequencing apparatus, or nanopore sequencer a set of genetic variants in an organism, wherein each of said genetic variants is correlated with a medical care phenotype; using a computer to determine the predisposition or carrier status of said organism for at least two phenotypes, wherein said predisposition or carrier status is based on said set of genetic variants; providing a report of said predisposition or carrier status to said organism, to a health care provider of said organism, or to a third party; and, optionally, (d)combining the predisposition or carrier status of said organism for said at least two phenotypes into a Medical Care

score, wherein said score is reported to said organism, to a health care provider of said organism, or to a third party.

[0052] In an embodiment of the medical care aspect, at least two phenotypes comprise an initial phenotype and a reflex phenotype, wherein said reflex phenotype is a phenotype that is not the initial phenotype, and wherein the reporting of the predisposition or carrier status of said organism for the reflex phenotype depends on the outcome of said determination of predisposition or carrier status of said organism for the first phenotype. In some embodiment, at least two phenotypes are at least two phenotypes listed in one or more of FIGS. 15-20 . In another embodiment, at least two phenotypes comprise: at least one phenotype that follows monogenic inheritance; and at least one phenotype that follows multifactorial or polygenic inheritance.

[0053] In an embodiment of the medical care aspect, wherein said at least two phenotypes comprise an initial phenotype and a reflex phenotype, said reflex phenotype is reported when said organism has an increased predisposition or carrier status for said initial phenotype. In some embodiments, said reflex phenotype is reported when said organism has a decreased predisposition or carrier status for said initial phenotype. In other embodiments, said reflex phenotype is not reported if the organism has neither a decreased or increased predisposition or carrier status for said initial phenotype. In further embodiments, said reflex phenotype is reported concurrently with said initial phenotype. In another embodiment, said reflex phenotype is reported subsequently to said initial phenotype.

[0054] In an embodiment, wherein at least two phenotypes comprise an initial phenotype and a reflex phenotype, wherein said reflex phenotype is a phenotype that is not the initial phenotype, and wherein the reporting of the predisposition or carrier status of said organism for the reflex phenotype depends on the outcome of said determination of predisposition or carrier status of said organism for the first phenotype, wherein the determination of the predisposition or carrier status of the organism for said reflex phenotype is determined subsequently to the determination of the predisposition or carrier status of the organism for said initial phenotype.

[0055] In some embodiments of the medical care aspect, said reflex phenotype is a disease that is positively correlated with said initial phenotype. In other embodiments, said initial phenotype is a disease and said reflex phenotype is a symptom of said disease. In further embodiments, said initial phenotype is a disease or disorder and reflex phenotype is a side effect of, or response to, a treatment for said initial phenotype.

[0056] In an embodiment, a method of determining the predisposition or carrier status of an organism for two or more phenotypes related to Medical Care is provided, wherein said two or more phenotypes are selected. In some embodiments, said set of genetic variants is identified using a high density DNA microarray. In other embodiments, said set of genetic variants is identified by sequencing genomic DNA from said organism. In further embodiments, said organism is a subject of one or more genetic panels of the invention. In another embodiment, said organism is suffering from an unknown

disease or condition. In yet another embodiment, said organism is an organ, cell, or tissue transplant candidate. In another embodiment, said organism has died of unknown causes.

[0057] In another medical care aspect, a medical care set of probes is provided, wherein said set comprises probes, wherein each of said probes is specifically selected to detect a genetic variant correlated with a medical care phenotype. In an embodiment of the medical care set of probes, said set detects at least two phenotypes listed in FIGS. 15-20. In some embodiments of the medical care set of probes, said set comprises at least two probes, and each of said at least two probes detects a different genetic variant, and wherein each of said different genetic variants is correlated to the same phenotype.

[0058] In a third medical care aspect, a method is provided comprising: obtaining by nucleic acid array, sequencing apparatus, or nanopore sequencer a set of genetic variants for one or more subjects, wherein said one or more subjects have been or are contemplated to be in a clinical drug efficacy or safety trial, and wherein each member of said set of genetic variants is identified with each of said one or more subjects and wherein each member of said set of genetic variants is also correlated with a phenotype; obtaining clinical trial results data for said one or more subjects, or providing clinical trial results data previously obtained for said one or more subjects, wherein each of said clinical trial results are identified with each of said one or more subjects; and using a computer to correlate the clinical trial results identified with each subject with the set of genetic variants identified with each subject; wherein the step of correlating identifies one or more of said genetic variants that are predictive for one or more of said clinical trial results. In an embodiment of the method, the method further comprises identifying one or more subsets of subjects that have a set of genetic variants that provide an increased chance of a positive or negative clinical trial result. In some embodiments, said clinical trial results indicate the level of safety of said clinical drug. In other embodiments, said clinical trial results indicate the level of effectiveness of said clinical drug. In further embodiments, said clinical trial results indicate the degree of adverse effects of said clinical drug.

[0059] In another embodiment of the third medical care aspect, said set of genetic variants comprises one or more genetic variants correlated with a phenotype listed in the Research & Clinical Trial Panels.

[0060] Another aspect provided herein is related to longevity or lifecycle phenotypes and is a method of determining the predisposition or carrier status of an organism for two or more longevity or lifecycle phenotypes comprising: identifying by nucleic acid array, sequencing apparatus, or nanopore sequencer a set of genetic variants in an organism, wherein each of said genetic variants is correlated with a longevity phenotype; using a computer to determine the predisposition or carrier status of said organism for at least two phenotypes, wherein said predisposition or carrier status is based on said set of genetic variants; providing a report of said predisposition or carrier status to said organism, to a health care provider or owner of said organism, or to a third party; and optionally combining the predisposition or carrier status of said organism for said at least two phenotypes into a longevity

score, wherein said score is reported to said organism, to a health care provider, or owner, or to a third party.

[0061] In an embodiment of the longevity phenotype aspect, at least two phenotypes comprise an initial phenotype and a reflex phenotype, wherein said reflex phenotype is a phenotype that is not the initial phenotype, and wherein the reporting of the predisposition or carrier status of said organism for the reflex phenotype depends on the outcome of said determination of predisposition or carrier status of said organism for the initial phenotype. In further embodiments, at least two phenotypes comprise: at least one phenotype that follows monogenic inheritance; and at least one phenotype that follows multifactorial or polygenic inheritance.

[0062] In further embodiments of the longevity phenotype aspect, said reflex phenotype is reported when said organism has an increased predisposition or carrier status for said initial phenotype. In another embodiment, said reflex phenotype is reported when said organism has a decreased predisposition or carrier status for said initial phenotype. In yet another embodiment, said reflex phenotype is not reported if the organism has neither a decreased or increased predisposition or carrier status for said initial phenotype. In some embodiments, said reflex phenotype is reported concurrently with said initial phenotype. In other embodiments, said reflex phenotype is reported subsequently to said initial phenotype. In further embodiments, the determination of the predisposition or carrier status of the organism for said reflex phenotype is determined subsequently to the determination of the predisposition or carrier status of the organism for said initial phenotype. In another embodiment, said reflex phenotype is a disease that is positively correlated with said initial phenotype.

[0063] In yet another embodiment of the longevity phenotype aspect, said initial phenotype is a disease and said reflex phenotype is a symptom of said disease. In an embodiment, said initial phenotype is a disease or disorder and reflex phenotype is a side effect of, or response to, a treatment for said initial phenotype.

[0064] In other embodiments of the longevity phenotype aspect, said two or more phenotypes are selected. In further embodiments, said set of genetic variants is identified using a high density DNA microarray. In another embodiment, said set of genetic variants is identified by sequencing genomic DNA from said organism.

[0065] Provided herein is a Research and Clinical trial aspect and is a method of determining the predisposition or carrier status of an organism for two or more Research and Clinical Trial phenotypes comprising: identifying by nucleic acid array, sequencing apparatus, or nanopore sequencer a set of genetic variants in an organism, wherein each of said genetic variants is correlated with a Research and Clinical Trial phenotype; using a computer to determine the predisposition or carrier status of said organism for at least two phenotypes, wherein said predisposition or carrier status is based on said set of genetic variants; providing a report of said predisposition or carrier status to said organism, to a health care provider of said organism, researcher, company, or to a third party; and, optionally,

combining the predisposition or carrier status of said organism for said at least two phenotypes into a Research and Clinical Trial score, wherein said score is reported to said organism, to a health care provider of said organism, a researcher, or a company, or to a third party.

[0066] In an embodiment of the Research and Clinical trial aspect, at least two phenotypes comprise an initial phenotype and a reflex phenotype, wherein said reflex phenotype is a phenotype that is not the initial phenotype, and wherein the reporting of the predisposition or carrier status of said organism for the reflex phenotype depends on the outcome of said determination of predisposition or carrier status of said organism for the first phenotype. In other embodiments, at least two phenotypes comprise at least five phenotypes. In further embodiments, at least two phenotypes comprise: at least one phenotype that follows monogenic inheritance; and at least one phenotype that follows multifactorial or polygenic inheritance.

[0067] In further embodiments of the Research and Clinical trial aspect, said organism is a research subject. In another embodiment, said organism is a suffering from an unknown disease or condition. In yet another embodiment, said organism is an organ, cell, or tissue transplant candidate. In an embodiment, said organism has died of unknown causes.

[0068] A second Research and Clinical trial aspect provided herein is a research and clinical trial set of probes, wherein said set comprises probes, wherein each of said probes is specifically selected to detect a genetic variant correlated with a Research and Clinical Trial phenotype. In some embodiments of the research and clinical trial related set of probes, said set comprises at least two probes, and each of said at least two probes detects a different genetic variant, and wherein each of said different genetic variants is correlated to the same phenotype.

[0069] A third Research and Clinical trial aspect provided herein is a method comprising: obtaining by nucleic acid array, sequencing apparatus, or nanopore sequencer a set of genetic variants for one or more subjects, wherein said one or more subjects have been or are contemplated to be in a clinical drug efficacy or safety trial, and wherein each member of said set of genetic variants is identified with each of said one or more subjects and wherein each member of said set of genetic variants is also correlated with a phenotype; obtaining clinical trial results data for said one or more subjects, or providing clinical trial results data previously obtained for said one or more subjects, wherein each of said clinical trial results are identified with each of said one or more subjects; and using a computer to correlate the clinical trial results identified with each subject with the set of genetic variants identified with each subject; wherein the step of correlating identifies one or more of said genetic variants that are predictive for one or more of said clinical trial results. In some embodiments of the method, the method further comprises identifying one or more subsets of subjects that have a set of genetic variants that provide an increased chance of a positive or negative clinical trial result. In other embodiments, said clinical trial results indicate the level of safety of said clinical drug. In further embodiments, said clinical trial results indicate the level of effectiveness of said clinical drug. In

another embodiment, said clinical trial results indicate the degree of adverse effects of said clinical drug.

INCORPORATION BY REFERENCE

[0070] All publications and patent applications mentioned in this specification are herein incorporated by reference to the same extent as if each organism publication or patent application is specifically and organismly indicated to be incorporated by reference in its entirety. This application incorporates by reference PCT Application No. PCT/US2009/01733, entitled "Genetic Analysis", filed on March 18, 2009.

BRIEF DESCRIPTION OF THE DRAWINGS

[0071] A better understanding of the features and advantages of the present invention will be obtained by reference to the following detailed description that sets forth illustrative embodiments, in which the principles of the invention are utilized, and the accompanying drawings of which:

[0072] **FIG. 1** illustrates an overview of some methods or business methods of providing genetic testing, profiles, and/or analysis.

[0073] **FIG. 2** depicts a diagram of a sample genetic pedigree, illustrated herein for a human organism. A male organism (proband) is identified on the pedigree by the arrow. The organism's maternal grandfather died from unknown cancer at age 55 and an uncle, on his maternal side, died from prostate cancer at age 58. His paternal grandparents both died in their 50's from unknown illnesses, a paternal uncle died of heart disease around the age of 60, and his father died recently of a heart attack at the age of 72. His mother has glaucoma and arthritis but is otherwise healthy and his sister and her two children are also healthy. No other family history is given. Genetic Pedigree Analysis may be utilized for genetic counseling. The same genetic pedigree analysis can be applied to nonhuman organisms as well. The pedigree may enable veterinary healthcare professionals, , to follow disease trends and identify possible at-risk organisms. Additionally, such information may be of use by animal husbandry specialists for breeding purposes. For non-human organisms, males are represented by squares, females as circles, and a line connecting a square and a circle from two different lineages represents a mating.

[0074] **FIG. 3** illustrates a Punnett Square where both parents are carriers of a monogenic disease. Normal Allele refers to the allele that is not associated with the phenotype (such as a disease). Disease Allele refers to the allele that is associated with the phenotype (such as a disease). Carrier means the organism possesses one phenotype-associated allele but does not have the phenotype. The organism may pass on a phenotype-associated allele to future generations. Diseased means the organism is 'Affected' or 'Likely to be Affected' by the phenotype. The organism may pass on a phenotype-associated allele to future generations. 'Carrier status' may refer to either being a 'carrier' or being 'affected or likely to be affected' by a phenotype.

[0075] **FIG. 4** depicts an information chart for a subject organism with **A)** limited information about the subject and **B-C)** with more information about the subject.

[0076] **FIGS. 5A and 5B** depict a sample report of genotypic data. “Rs” numbers are used when the genetic variant and its surrounding sequence has been included in the public United States’ National Center for Biotechnology Information’s (NCBI) dbSNP database (accessible at www.ncbi.nlm.nih.gov/SNP/) and assigned an “rs number”. If that specific genetic variant is not included in this public dbSNP database, then the genetic variant and its flanking sequence is assigned an “eg” number, which serves as an internal identification number. The genotype column denotes the diploid genotype for that variant (e.g. a genotype of “GA” denotes a heterozygous sequence of guanine and adenine at the position identified by the given variant), DEL denotes a deletion, and INS denotes an insertion. The data shown represents genetic variants for human organisms. The sample reports for non-human organisms may be generated in a similar manner.

[0077] **FIGS. 6 A-G** illustrate sample internal data reports as well as examples by which these reports can be filtered, such as for **A)** all conditions or traits, **B)** $GVP \geq 1.5$, **C)** monogenic, **D)** replicated or monogenic conditions, or **E-G)** phenotypes (“CSR” refers to Clinical Significance Rating; “PIR” refers to Phenotype Impact Rating). The particular phenotypes, conditions or traits described may be illustrative of human disease or may be illustrative of non-human organism disease. If the phenotype, condition or trait is illustrative for human disease only, it is described herein to demonstrate the methods of analysis to be applied to non-human organism disease states. For **FIG. 6 A-D: Column 1 = Genetic Variant**= identifies the specific genetic variant detected. “Rs” numbers are used when the genetic variant and its surrounding sequence has been included in the public National Center for Biotechnology Information’s (NCBI) dbSNP database (accessible at www.ncbi.nlm.nih.gov/SNP/) and assigned an “rs number”. If that specific genetic variant is not included in this public dbSNP database, then the genetic variant and its flanking sequence is assigned an “eg” number, which serves as an internal identification number.

[0078] **Column 2 = Genotype** = identifies the specific genotype detected during genetic testing for each of the genetic variants in column 1.

[0079] **Column 3 = Gene or Locus** = identifies the gene where the genetic variant (from column 1) occurs within or bordering. If the genetic variant occurs within an intergenic region, then the loci where the genetic variant exists is identified.

[0080] **Column 4 = Phenotype** = identifies the phenotype associated with the genetic variant (column 1) and its genotype (column 2). This association is ascertained from scientific literature.

[0081] **Column 5 = Phenotype-Associated Genotype or Allele** = identifies the allele or the genotype associated with the risk value for that phenotype. This information is ascertained from scientific literature.

[0082] **Column 6 = Population Match?** = identifies whether or not the organism’s population (such as gender, variety, breed, etc.) matches the population from scientific studies in which the genotype-phenotype association is deduced.

[0083] **Column 7 = Monogenic?** =identifies whether the genotype-phenotype association is monogenic or not. This information is ascertained from scientific literature.

Column 8 = Monogenic Status = identifies the status (affected or carrier) of monogenic phenotypes.

[0084] **Column 9 = Risk** =The risk value associated with the allele or genotype for the genotype-phenotype association. This is ascertained from scientific literature.

[0085] **Column 10 = Risk Type** =This identifies the type of risk value from column 8, such as whether it is an odds ratio (OR), relative risk (RR), or hazard ratio (Z). This is ascertained from scientific literature.

[0086] **Column 11 = Absolute Value** =this is either an absolute or cumulative value for this genetic variant's specific genotype-phenotype association, as reported in the scientific literature. An example of an absolute value is the new lifetime risk for that organism based on that genotype or an absolute amount associated with the phenotype (as opposed to an odds ratio, relative risk, or hazard ratio), such as a specific genetic variant's genotype being associated with an average systolic blood pressure of 140 mmHg $\pm$ 5 mmHg. In the example of blood pressure, if the blood pressure value is in the hypertensive range, then this would contribute to the CGR and PMR for hypertension as described herein.

[0087] **Column 12 = Absolute Value Descriptor** =this identifies exactly what the absolute or cumulative value (from column 11) is. For example, it can be "Cumulative Value" if the value listed in column 11 is a cumulative value, or it can be a lifetime risk at a specific age or age range, if the value listed in column 11 is a lifetime risk at a specific age or age range.

[0088] **Column 13 = Replicated** =this identifies whether or not the genetic variant's genotype-phenotype association and its risk value or absolute value has been replicated. If it has been replicated (two or more independent studies have found the same statistically significant genotype-phenotype association and the same direction of risk) then it is assigned a "Yes", if it has not been replicated yet, then it is assigned a "No", if it is replicated within a single study (such as if two independent populations were found to have the same statistically significant genotype-phenotype association and the same direction of risk) then it is assigned a "Within" and if the genotype-phenotype association is a monogenic phenotype, then it is assigned "Mono". If the genetic variant's genotype-phenotype association is not found to be statistically significant in subsequent studies after a study has found it to be statistically significant, then it is assigned "Failed". If there are three or more studies, where one or more contains data that is contradictory to the other studies (such as if two studies find a statistically significant association between a genetic variant's allele or genotype and a phenotype but a third does not) for the same population, then the studies with the highest power (number of organisms in the study cohort) are considered most relevant.

[0089] **Column 14= GVP Score** =the GVP Score means the 'Genetic Variant-Phenotype Score', which is a value for the degree to which that genetic variant has been replicated in the scientific literature. The description for GVP score appears in **FIG. 7**.

[0090] **Column 15 = GVP Triage** =the GVP Triage means the ‘Genetic Variant-Phenotype Triage’, which is a value that discerns its clinical significance. The descriptions for GVP Triage appear in FIG. 8.

[0091] **Column 16= GVP Rank** =the GVP Rank is the order in which that genetic variant should be utilized in case two or more genetic variants within tight linkage disequilibrium are both detected during genetic testing. If these genetic variants are associated with the same signal, they may give the same risk information about the phenotype association and only one should be included in the calculations and algorithm. The genetic variant designated with a GVP Rank of “1” will always be utilized first, over any other rank. For example, if two genetic variants (X and Y) within the same gene or locus were both detected and both provide the same signal information about the phenotype (as ascertained from the scientific literature or HapMap linkage disequilibrium data or both), and genetic variant X is ranked 1 and Y is ranked 2, only genetic variant X will be utilized in the calculations and algorithm. Genetic variant Y may still also be tested for and/or analyzed because it may give other information about another phenotype, it may be part of a haplotype, it may be part of a panel of variants that are tested and/or analyzed, or the data may be obtained as a consequence of obtaining the data for genetic variant X. If only genetic variant Y is detected but genetic variant X is not, then that means genetic variant Y, with a GVP Rank of 2, will then be used in the calculations and algorithm.

[0092] **FIG. 7** illustrates a sample of a Genetic Variant-Phenotype (GVP) scoring scheme.

[0093] **FIG. 8** illustrates a sample of a Genetic Variant-Phenotype (GVP) Triage scoring scheme.

[0094] **FIG. 9** is a CGR Multiplier and PMR (Predictive Medicine Risk) or NRV (No Risk Value) Multiplier chart.

[0095] **FIG. 10** is an example of a chart for scores by organ system and an overall genetic health score. The Cumulative Action Score (CAS) can be filled in for more than one organ system and determined for an organ system. The organ system score or Indicator of Genetic Health of an Organ System can be indicated by a color. Red can be used for scores less than -10, indicating high importance for discussion with the subject’s caretaker and may be highly important for the caretaker to follow-up with a veterinary health professional or animal husbandry specialist based on this information, pink can be used for scores between -1 to -10 to indicate moderately important risk, green can be used for scores of 0 to indicate no pertinent deleterious or protective information discovered although organ system is accessed, blue can be used for scores between +1 to +10, to indicate moderately important protection, gold can be used for scores >+10 indicating very beneficial protection, and no color can be used for an Organ System or Medical Specialty if it is not accessed. The overall genetic health score can be determined by adding all the CAS and dividing by the total number of CASs, which may be used as an indicator for genetic wellness and is also represented by a color as is the Indicator of Genetic Health of an Organ System. Although **FIG. 10** illustrates a chart that can be used for humans, similar charts may be used or adopted for non-human organisms.

[0096] FIGS. 11A and 11B depict a schematic of a computer system useful in the methods of the present invention. **FIG. 11A** is a schematic of a non-limiting example of a computer system that can be used for storing, receiving and analyzing data from genetic results or testing. **FIG. 11B** is a schematic of a non-limiting example of the general steps for obtaining a genetic analysis of a subject sample from a computer system that can be used for receiving and analyzing genetic data.

[0097] FIGS. 12A to 12G depict reports that are generated from a subject that is tested with a full genome analysis panel, illustrated herein for a human. The exemplary reports include **A-B**) Risk Assessment reports for Alzheimer's Disease (**A**) and Macular Degeneration, Age-Related (**B**), **C-D**) Carrier Assessment reports for Malignant Hyperthermia (**C**), and Cystic Fibrosis (**D**), **E**) Healthcare Professional Summary and **F-G**) References. For a non-human subject, either the same or different diseases may be the subject of the reports. The Healthcare Professional Summary may be directed to either a veterinary professional or an animal husbandry specialist. The references may refer specifically to the disease state in a specific non-human organism or may include references concerning human disease wherein the results may be extended to a non-human organism.

[0098] FIGS. 13A to 13F reflex testing schematics of **A**) general reflex testing; **B**) a panel for obesity and leanness, and **C**) a carrier screening panel (rare diseases, orphan diseases, metabolic diseases and/or syndromes); **FIG. 13 D** depicts a general matrix reflex testing schematic; and **FIGS. E-F** depict matrix reflex testing schematics of **E**) general prostate cancer and of **F**) Epidermolysis Bullosa Simplex (EBS). While these panels are illustrated for a human subject, similar reflex schematics can be prepared for non-human subjects/organisms.

[0099] FIGS. 14A and 14B depict schematics for the 2 part analysis for Offspring Projection through the Combined Analyses of Different Individuals (OP-CADI).

[0100] FIGS. 15A to 15DD depict panels relevant to cattle, including General Cattle Panel (15A to 15D); Cattle Dairy Panel (15D to 15G); Cattle Disease Panel (15H); Cattle Growth Panel (15H to 15I); Cattle Lifecycle and Economic Productivity Panel (15I to 15L); and Cattle Meat Panel (15M to 15BB).

[0101] FIGS. 16A to 16I depict panels relevant to chickens, including General Chicken Panel (16A to 16B); Chicken Disease Panel (16B to 16C); Chicken Egg Panel (16C); Chicken Growth Panel (16C to 16D); Chicken Immune System Panel (16D);); Chicken Lifecycle and Economic Productivity Panel (16D to 16F); and Chicken Morphology Panel (16F to 16G); and Chicken Reproduction Panel (16G to 16H).

[0102] FIG 17A to 17J depict panels relevant to dogs, including General Dog Panel (17A); Companion Panel (17A to 17C); Dog Conformation Events Panel (17C to 17D); Dog Disease Panel (17D to 17E); Dog Herding and Hunting Panel (17E); Dog Law Enforcement Panel (17E to 17F); Dog Learning and Intelligence Panel (17F); Dog Morphology Panel (17F to 17G); Dog Racing Panel (17G); and Dog Research & Clinical Study Panel (17G to 17J).

[00103] FIGS. 18A to 18D depict panels relevant to horses, including General Horse Panel (18A); Horse Lifecycle and Economic Productivity Panel (18A-18B); Horse Morphology Panel (18B); Horse Racing/Sports Panel (18B); Horse Reproduction Panel (18B); and Horse Worker Panel (18C-18D).

[00104] FIGS. 19A to 19I depict panels relevant to pigs, including General Pig Panel (19A to 19C); Pig Meat Panel (19C to 19D); Pig Morphology Panel (19D to 19E); Pig Reproduction Panel (19E); Pig Disease Panel (19E to 19F); and Pig Lifecycle and Economic Productivity Panel (19F to 19H).

[00105] FIG. 20 depicts a General panel relevant to sheep.

[00106] FIG. 21 depicts various options for selection of phenotypes from panels, such as Offspring Projection through the Combined Analyses of Different Organisms (OP-CADI) Option, Only Decreased Risk Option, Only Increased Risk Option, or Specific Disease Exclusion Option.

[00107] FIG. 22A to 22Q depicts significant genetic variants and their associated disease or trait.

[00108] FIG. 23A to 23C depict example indications that, if present, may suggest genetic testing using the specified panel.

[00109] FIG. 24 illustrates multifactorial phenotype risks which have, for example, both a genetic component and a non-genetic factor as compared to monogenic or polygenic phenotype risks.

DETAILED DESCRIPTION

[00110] Genotypes contribute to phenotypes, such as traits, diseases, disorders, conditions, or characteristics. Genotypes comprising genetic variations, such as allelic polymorphisms or single nucleotide polymorphisms (SNPs), can provide a method of correlating a genotype with one or more phenotypes for an organism. For example, clinically relevant polymorphisms can be used to determine clinically relevant phenotypes, including phenotypes such as the risk or predisposition an organism has for a specific disease, disorder, condition, or trait. Phenotypes may also include the pharmacogenomic profile of an organism including medication metabolism, effectiveness, adverse reactions, dosing indications, and choice of medication. Many phenotypes, such as diseases, disorders, traits and conditions are multifactorial and may be interconnected with other phenotypes. Monogenic disorders can also be interconnected with other phenotypes. A comprehensive, dynamic analysis of an organism genome, combined with non-genetic factors, can be used to understand the organism's risk or predisposition, carrier status, diagnosis, determination and risk or predisposition to future generations of monogenic, polygenic and multifactorial phenotypes, as well as their interconnectedness with other relevant phenotypes.

[00111] Provided herein are methods and systems for generating genetic profiles

[00112] The term "genetic profiles" includes genetic analyses and/or genotype profiles. The genetic profiles can provide comprehensive, dynamic genetic analysis for an organism. Genetic profiles can use genetic information from an organism to determine the carrier status of a phenotype or a predisposition or risk for a phenotype. Organisms may be human as well as non-human, such as other mammals, including, but not limited to pets, such as dogs, cats, and birds; farm animals such as pigs,

cattle or cows, goats, chickens, turkeys, ducks, turkey, fish, and sheep, as well as other animals, such as apes, bison, camels, , (for example, racehorses, such as Harness and Thoroughbred), whales and dolphins. In some cases, the disclosure applies to human organisms. In some cases, the disclosure applies to non-human organisms. In some cases, the disclosure applies to mammals or non-human mammals. Genetic profiles may also be generated for plants, including but not limited to cotton plants, olive trees, evergreen coniferous trees, banana trees, apple trees, orange trees, grapefruit trees, cherry trees, almond trees, wheat, corn, hemp, soybeans and rice. Genetic profiles can be generated for fish, including but not limited to salmon, tuna, sea bass, Alaska pollock, cod, eels, tilapia, flashlight fish, anglerfish or sharks. Genetic profiles can also be generated for invertebrates, such as lobsters, shrimp, scallops and insects; fungi; microorganisms, such as bacteria or viruses; and endangered species or extinct species from which genetic material can be obtained.

[00113] A phenotype is any observable, detectable or measurable characteristic of an organism, such as a condition, disease, disorder, trait, behavior, biochemical property, metabolic property or physiological property. The genetic information can also be used to determine the pharmacogenomic profile for an organism. The genetic information can also be used to determine the likelihood or predisposition of an organism or a couple in passing on genes and genetic variants that may contribute to specific phenotypes in their offspring or the likelihood of specific phenotypes occurring in potential offspring through the genetic analysis of different organisms as potential parents. The information may also be used in a second analysis or determination of an organism's carrier status of a phenotype or their risk or predisposition to a phenotype. Knowledge of the risks can be useful to health care providers in evaluating health risks, such as by providing recommendations to improve an organism's health or preventive medicine recommendations that may help decrease the incidence, or delay the onset, of specific diseases in that organism's future. Recommendations may include medical recommendations, as well as recommendations that may include, but are not limited to, changing habits, such as dietary changes, exercise regimens, levels of stress and stress reduction and the like. Risks or predispositions can be reflected by scores or other numerical values. For example, the score or numerical value may be scaled to express the level of risk or predisposition to a phenotype, such as a medical condition or a non-medical condition.

[00114] **FIG. 1** illustrates some general and non-limiting steps involved in genetic analysis. Samples or specimens, such as any biologic specimen or biologic material, may be taken at the central location (104) and after or before payment, submitted for processing (112 or 116) at a sample processing facility (108) such as a laboratory (158) that may processes the sample, conduct the genetic testing and/or generate the results (such as raw genotypic data or genetic analysis) (120, 156, 144). The laboratory (158) may or may not adhere to appropriate governmental agency guidelines and requirements, for example, in the United States, a processing laboratory may be regulated by one or more federal agencies such as the Food and Drug Administration (FDA) or the Centers for Medicare and Medicaid Services (CMS), and/or one or more state agencies. In the United States, a clinical

laboratory may be accredited or approved under the Clinical Laboratory Improvement Amendments of 1988 (CLIA). Samples may also be obtained from organisms at other locations such as health care facilities (110) or directly from the organisms themselves (102, 134). Samples may also be obtained from other channels or facilities (114), e.g., DNA storage bank, blood bank, tissue bank, tissue repository, crime scene, pathology laboratory, morgue, archeological site, or other location. For example, 'ancient DNA' may be found at an archeological dig site. Thus, at times, the actual 'organism', such as a person or animal or other organism, may not actually be present when the sample is collected. In some embodiments, the nucleic acid may be provided from the organism, or third party, as a sample, which sample may have been previously obtained, i.e. prior to performance of the method of the invention (102).

[00115] Other channels or facilities (114) also may include facilities such as spas, medical spas, gyms, fitness centers, weight loss centers, clinics, kiosks, nurses offices, schools, governmental agencies or offices, programs, crime scenes, prisons, jails, military locations, ambulances, hospitals, medical centers, doctor's office, clinics, fertility centers, assisted reproductive technologies centers, sperm banks or donation centers, egg donation centers or programs or companies, prenatal testing companies, business locations, corporate locations, bench research centers, clinical research centers, pharmaceutical companies, places of military, police, or clandestine operations, an organism's house, wellness centers, in the wild, at an owner's home, at an owner's place of business, at a corporation, at a governmental facility, at a supermarket, at a food processing center, at a food quality control center, longevity centers, space centers, executive health programs, funeral homes, veterinarian's offices, veterinary clinics, veterinary hospitals, farms, ranches, natural habitats, archeological digs, archeological centers, museums, cemeteries, or industrial locations. Such facilities may themselves collect samples or specimens (112, 116) from organisms or animals or any organism or from the sample's place of occupancy as stated herein and submit to a central (104) location after or before payment, where the samples are then submitted to a laboratory (158), such as a CLIA laboratory or a non-CLIA laboratory, for processing. Alternatively, the sample may be sent directly from the place of sample collection (104, 110, 114, 134) to a laboratory (158) (either CLIA or non-CLIA certified laboratory) where the genetic testing and/or genetic analysis then occurs or the sample may undergo genetic testing and/or genetic analysis at the sample collection site (104, 110, 114, 134) itself. Optionally, before the testing or analysis of his or her genome, an organism's owner may receive "pre-test" genetic counseling (106). Following such counseling, the specimen may be sent to a CLIA or NON-CLIA laboratory (108). In some cases, an organism's owner, caretaker, or representative of organism may send the organism's genetic testing results directly to the Central Location (146), where such results may be further analyzed, compiled into a report, and sent or transmitted back to the organism (148). Results may refer to genotypic data ascertained at any time point, such as concurrently or anytime in the past, and may refer to genotypes at one or more genetic variants.

[00116] As also illustrated in **FIG. 1**, a physician, veterinarian, or other healthcare professional (110) may obtain a biological specimen from a subject organism, third party or animal (150, 152) and may send it to either a central location (112, 104) or to a laboratory (154, 158) for genetic testing and/or analysis in order to ascertain the genotype of one or more genetic variants throughout the genome and, optionally, in order to correlate the genotype with one or more phenotypes. The central location or laboratory may also be a site where methylation status, epigenetic factors at one or more genetic variants throughout the genome, karyotype and/or cytogenetic properties are evaluated. The results of the genetic testing or the genetic analysis (e.g., a genetic analysis contained in a genetic report) (124) may then be sent and/or transmitted to the veterinarian, health care professional, animal husbandry specialist, and/or the caretaker of the organism (110). Alternatively, the genetic testing may have already been completed, either at the time or in the past, and the results of the genetic testing, such as genotypic results may then be sent or transmitted to a central location or analytical IT system (112) where genetic analysis may be performed. The genetic analysis (such as a genetic report) may then be sent or transmitted (124) to the veterinarian, health care professional, animal husbandry specialist, and/or the caretaker of the organism (110) or to another location (114).

[00117] A consumer, caretaker of an organism, or third-party (134) may collect a biological specimen from the organism on his or her own as described herein and send the specimen (138) to the laboratory (158). The laboratory may then perform genetic testing on genetic material isolated from the biological specimen (or the biological specimen may already be genetic material, such as isolated DNA) in order to determine one or more genetic variants throughout the genome and will send and/or transmit the results and/or the analysis (such as a genetic report, if the laboratory also conducts the analysis) back to the consumer, caretaker of the organism or third party (140). If the laboratory does not conduct the analysis, then the laboratory (158) may send the genetic testing results (120) to a central location and/or analytical IT system (104) that then may conduct the genetic analysis and may send the analysis either back to the laboratory (118) that may then return the analysis (140) to the consumer, caretaker of the organism, or third party (134) or the central location and/or analytical system may send or transmit the analysis (148) (such as a genetic report) to the consumer, caretaker of the organism, entity, or patient (134). Alternatively, the consumer, caretaker of the organism, or third party (134) may already have results from genetic testing (such as from current or recent genetic testing or genetic testing done anytime in the past) and may send the results of this genetic testing (146) to a central location and/or Analytical IT System (104) that then may analyze the results and send or transmit or both the analysis (such as a genetic report) (148) to the consumer, caretaker of the organism, or third party (134).

[00118] Any results obtained at the Central Location (104), may also be sent to yet another location, where post-test predictive medicine genetic counseling is conducted (128). A genetic report describing genetic analysis or genetic tests and containing other information described herein may

then be sent or transmitted to the caretaker of the organism, or to another third party, such as the veterinarian or animal husbandry specialist of the organism (132).

[00119] A consumer, caretaker of the organism, third party and/or non-human species may either visit, or be taken to, a location that extracts a biological specimen (as described herein) or leave a biological specimen from the organism (136) at a location (114), either willingly (such as donating sperm to a sperm bank or donating a tissue sample to a tissue bank) or unwillingly (such as being a victim of a crime that leaves blood or other bodily fluid at the scene of a crime or a biological sample discovered at a place of archeological excavation and/or investigation) and this biological specimen may then be sent (142) to a laboratory (158) or the specimen may be sent (116) from the location (114) to a central location and/or analytical IT system (104) where it may undergo genetic testing (such as with a lab on a chip handheld device) or stored or the specimen may be sent (118) to a laboratory (158) to be stored or for testing. The results of the genetic testing may then be sent or transmitted (120) to a central location and/or analytical IT system (104) or to the consumer, caretaker of the organism, or third party (140, 134) or to the location (114).

[00120] The results may be analyzed at the central location and/or analytical IT system (104) and then the analysis (such as a genetic report) is sent and/or transmitted (126), back to the location (114), which may be the same location (such as a forensics laboratory) or a different location (such as a government building or a police station). The location (114) may also already have the results from current or previous genetic testing and may send or transmit the results (116) to a central location and/or analytical system (104) where the results are analyzed and then the analysis is sent or transmitted (126) back to the location (114), which can be the same location that sent the results or a different location (for example, the results may have been sent or transmitted (116) by a governmental agency (114) and the analysis (such as a genetic report) is sent or transmitted the Department of Agriculture (114), or the analysis can be sent or transmitted or both to more than one location, such as to the governmental agency (114), the Department of Agriculture (114), the Food and Drug Administration (114), a farm or ranch (114) and/or a veterinarian's office (110). Genetic testing results or analysis (such as a genetic report) or both may be sent or transmitted or both back to the same location that sent the specimen or to a different location or they may be sent or transmitted to multiple locations at once or at different times. The genetic specimen may also be stored at various locations (104, 110, 114, 158, 134) for a defined amount of time (such as one year) or indefinitely. The results or the analysis or both may also be stored at various locations (104, 110, 114, 158, 134) for a defined amount of time (such as one year or five years or ten years or 20 years or 50 years or 100 years) or indefinitely.

[00121] Alternatively, the laboratory (158) may refer to a desktop device or machine that exists within the field or an office or home setting, or other location, such as within the office where the biologic sample is taken or received or both (102, 104, 110, 114, 134, 150, 158). The laboratory may also refer to a handheld device that analyzes either the purified DNA sample or the unprocessed biologic

specimen or both, as is currently being developed, such as “lab on a chip” technology (see for example, Karlinsey and Landers, Lab Chip, 8: 1285 (2008)). The genetic testing to ascertain specific alleles or genotypes or both of specific genetic variants or for partial exome, full exome, or full genome sequencing may occur on this desktop or hand-held device or the analysis itself of the genetic variants, their genotypes, and their association with phenotypes, or both, may either in part or in whole occur on the device, and the desktop or handheld device may display or print out all the results or a subset of the results of the genetic testing, such as specific phenotypes, such as the diagnosis or carrier status of specific diseases or traits or the risk of specific diseases or traits. Conducting genetic testing utilizing a desktop or handheld device may allow for rapid genotype or associated phenotypes to be analyzed and elucidated or both genotyping (genetic testing) and phenotyping (analysis), results to be reported, analyzed, understood, or conveyed to the healthcare provider or any person operating the device or requesting the testing or analysis or both. This may allow for rapid genetic testing, analysis, and genetic reports to be generated at the location of the organism, such as in the veterinary clinic, at an accident scene, such as by an emergency veterinary technician, at a business location, such as a feedlot by a feedlot attendant, at a security entrance or to confirm identity and to guard access to any location or material at any time, such as by an automated machine or by a security guard or by an immigration or customs official, at an organism’s home, such as by the organism’s owner or guardian, on a battle field, such as by a soldier or medic or military physician, a veterinarian, a provider of health care services to a non-human species, at investigator of a disease related to an animal product, such as food made from an animal, or at a crime scene, such as by a crime scene investigator, forensic investigator or medical examiner.

[00122] In some embodiments, the laboratory (158) processes the sample to isolate the genetic material needed for genetic testing and runs the genetic testing to generate a raw genetic genotype profile (that provides the genotypes or specific alleles at one or more places within the genome). The biological sample can be any sample from the organism in which genetic material may be isolated. Such biological samples include, but are not limited to, blood, hair, skin, saliva, semen, urine, fecal material, sweat, tears, buccal tissue, tongue cells, epithelial cells, and various bodily tissues (e.g., a buccal swab, hair follicle, saliva sample, semen sample, skin sample, epithelial cells, genetic material, DNA, or blood). The tissue or DNA sample may be directly collected by the organism (134), for example, a buccal or cheek sample may be obtained by the organism taking a swab against the inside of their cheek. Other samples such as a hair follicle, saliva, semen, skin, urine, fecal material, or sweat, may also be supplied by the organism’s owner or representative themselves (134). Other biological samples may be taken by a physician, veterinarian, or health care specialist, such as a phlebotomist, genetic counselor, nurse or physician, physician assistant, nurse practitioner, or other healthcare provider or specialist providing access to the genetic testing and analysis service (110, 104). For example, blood samples may be withdrawn from an organism by a nurse. Biological samples may also be taken by other organisms, such as, for example, a medical examiner, a police

officer, a crime scene investigator, an archeologist, a medic, or a government official (114). Tissue biopsies may be performed by a physician, veterinarian, or health care specialist (110), and kits may also be available to health care specialists to efficiently obtain samples. A small cylinder of skin or tissue may be removed or a needle or scalpel or swab or adhesive may be used to remove a small sample of tissue or fluids. Blood or other bodily fluid may be collected from a crime scene by swab or field kit or other collection apparatus by, for example, a detective, officer of the law, forensic investigator, or medical examiner (114).

[00123] The sample may be obtained at any time either at one of the locations described herein or at any other location not described herein. While the genetic testing of the sample (to obtain genotypic data) may have also occurred, either at a CLIA or non-CLIA laboratory or at any other location, such as the sample collection site (104, 110, 114, 134), in the past (so that some or all of the genotypic data may be already known) or may occur at the present time, such as at a CLIA or non-CLIA laboratory (158) or other facility or at the sample collection site itself, the genetic analysis of the genotypic data to ascertain phenotypic data may occur either at a separate time or at the same time as the genetic testing. The genetic analysis may occur at the same or different location from where the sample is obtained and the genetic analysis may occur at the same or different location from where the genetic testing occurred or is occurring and the. For example, the sample collection, genetic testing and analysis may all both occur at the health care professional's office (110) or the sample collection may occur at the health health care professional's office (110), the genetic testing may occur at a CLIA or non-CLIA laboratory (158), and the genetic analysis may then occur at a central location (104) or at the via interaction with a physician, veterinarian or healthcare professional, such as at a physician's or veterinarian's office (110). As another example, the sample collection, such as blood, may occur at a crime scene (114) years after the blood is actually left at that location and when the organism the blood is from is not currently present, the genetic testing may then occur at the present time at a central location (104), and the genetic analysis may occur immediately following the genetic testing, also at a central location (104) and then the results of either the genetic testing or the genetic analysis or both, such as contained within a genetic report, may then be conveyed to the organism or company or agency or governmental body that ordered the genetic testing (104) or the genetic analysis or both either immediately following the genetic testing and/or analysis or at a later time. Alternatively, the genetic testing or the genetic analysis or both may have occurred at a laboratory (158), such as a CLIA or non-CLIA laboratory.

[00124] Just as the specimen collection, genetic testing, and genetic analysis may all occur at the same location or at one or more different locations or all at different locations, the specimen collection, genetic testing, and genetic analysis may also all occur at the same time, at one or more different times, or at all different times. For example, specimen collection may occur at time A, with genetic testing occurring instantaneously or seconds, minutes, hours, days, weeks, months, years, decades, centuries, millennia later at time B and genetic analysis may then occur instantaneously as well or may occur

seconds, minutes, hours, days, weeks, months, years, decades, centuries, millennia later at time C. As another example, a biological sample detected in permafrost or a mummy from an archeological site may provide a sample of DNA that may be very old, referred to as 'ancient DNA', and this biological sample may then be sent to a laboratory (158) where genetic testing occurs with some initial preliminary analysis. However, the genetic testing results may then be stored for a number of years or decades and either the biological sample may undergo genetic testing again and then analyzed or the original genetic testing genotypic data may be reanalyzed at this later time point. The results of the genetic testing or genetic analysis or both may be stored or conveyed or both to the organism or agency or government who ordered or paid for the test, or both.

[00125] Reflex testing, OP-CADI (both of which are terms that are described further herein), and/or testing for specific phenotypes by utilizing specific genetic variants or panels may also apply to one or more of the following: desktop or handheld genetic testing and/or analysis and/or reporting. This type of laboratory (158) and/or handheld device may or may not fall under certain regulations, such as governmental regulations, or have to satisfy certain quality control, or governmental, requirements.

[00126] Phenotype include all subcategories of that phenotype. For example, the phenotype Fat Content of Milk in Cattle refers to the percentage fat content of milk, the fat yield of the milk, the fat yield over the duration lactation period, and/or the total fat content of the milk. Any possible way to measure the phenotype and/or convey the phenotype is contained within the phenotype name.

[00127] An organism's risk or predisposition for a phenotype may include his or her risk for a monogenic phenotype. In some embodiments, an organism's risk or predisposition for a phenotype includes his or her risk or predisposition for polygenic or multifactorial phenotypes. In such cases, the likelihood of developing a phenotype (e.g., disease, disorder, condition or trait) can be calculated based on an organism's alleles or genotypes for one or more genetic variants associated with polygenic or multifactorial phenotypes, and may also include analysis of non-genetic factors such as environment (non-genetic) factors.

[00128] Risk may also be referred to as a predisposition. Risks may also be expressed as a percentage for an indication of the likeliness of the chance event, such as a medically defined phenotype, such as a condition or a non-phenotype, such as a trait, to occur. Risks scores can also be provided with a confidence interval, a statistical value such as a p-value, Z-score, correlation (e.g. R or R²), chi-square, f-value, t-value or both a confidence interval and a statistical value, indicating the strength of correlation between the score and the condition or trait thereof. Scores can be generated for an organism's risks or predispositions for medical conditions based on an organism's genetic profile. Scores can be determined for a specific phenotype (e.g., disease, disorder, condition or trait), for an organ system, for a specific organ, for a combination of phenotypes, for a combination of phenotype(s) and organ(s) or organ system(s), for overall health, or for overall genetic predisposition to or risk of specific phenotypes. The phenotype may be a medical condition, for example, scores can be generated for an organism's risks or predispositions for medical conditions based on an organism's

genetic profile. Alternatively, scores can be for non-medical conditions, or for both medical and non-medical conditions. Scores may be generated by methods known in the arts, such as described in PCT Publication WO2008/067551 and US Publication No. 20080131887 (each of which is incorporated by reference in its entirety) methods such as described herein, or variations and combinations thereof. In some cases, the risks may be determined using a machine such as a general purpose computer or a special purpose computer using instructions provided on computer readable medium. Inclusion of the specific algorithms described herein to analyze the genetic information and calculate scores representing risks, predisposition to a phenotype and/or overall health profiles, for example, transform a general purpose computer into a special purpose computer for analyzing the genetic variants identified. Such algorithms can be provided in any combination to execute those functions desired by a client. Thus, the computer system may include some or all of the computer executable logic encoded on computer readable medium to instruct the computer system to complete the analysis, evaluations, scoring of the identified genetic variants, recommendations and reports for the client as desired.

[00129] In some embodiments, the calculated or determined risk or predisposition of one or more specific phenotypes from an organism's genetic profile provides a measure of the relative risk or predisposition of that organism for one or more phenotypes, as further described herein. The relative risk may be determined as compared to the general population or as compared to a control (e.g. a different organism) lacking one or more of the genetic variants identified in the organism's genetic profile. Additional examples and further description of risk and risk scores are provided herein.

[00130] In some cases, an organism with an increased relative risk or predisposition for a specific phenotype may be an organism with an odds ratio of greater than 1 for the specific phenotype, for example an organism with an odds ratio of about 1.01, 1.05, 1.1, 1.2, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25, 50, or 100 or more for developing a phenotype relative to the general population or a control organism. In some cases, an organism with an increased risk or predisposition may be an organism with a greater than 0% increased probability of a phenotype, for example an organism may have a 0.001% greater probability of a phenotype based on their genetic profile, a 0.01% greater probability, a 1% greater probability, a 5% greater probability, a 10% greater probability, a 20% greater probability, a 30% greater probability, a 50% greater probability, a 75% greater probability, a 100% greater probability, a 200%, 300%, 400%, 500% or more greater probability of a phenotype relative to the general population or a control organism. In some cases, an organism with an increased risk or predisposition may be an organism with a greater than 1 fold increased probability of a phenotype relative to a control organism or the general population such as for example about a 1.01 fold, 1.1 fold, 1.2 fold, 1.3 fold, 1.4 fold, 1.5 fold, 2 fold, 3 fold, 5 fold, 10 fold, 100 fold or more increased probability of a phenotype relative to a control organism or the general population. Increased risk or increased predisposition may also be determined using other epidemiological methods such as for example calculation of a hazard ratio or a relative risk.

[00131] In some cases, an organism with a decreased risk or decreased predisposition for a specific phenotype is an organism with an odds ratio of less than 1, for example 0.99, 0.9, 0.8, 0.7, 0.5, 0.4, 0.2, 0.1, 0.01 or lower odds ratio relative to a control organism or relative to the general population. An organism with a decreased risk or predisposition for a specific phenotype may be an organism with a lower percentage probability than a control organism or the general population for a phenotype. For example, the organism may have a 0.1% lower risk, 1% lower risk, 5% lower risk, 10% lower risk, 15% lower risk, 25% lower risk, 30% lower risk, 40% lower risk, 50% lower risk, 75% lower risk, or 100% lower risk than a control organism or the general population for a phenotype. An organism's decreased risk or predisposition may also be determined as a hazard ratio or a relative risk.

[00132] An organism's genetic profile and scores can be used by third parties such as for example, genetic counselors (GCs) and medical professionals such as, for example, physicians, physician assistant, nurse practitioner and medical specialists, or veterinarians (if the genetic testing is conducted on animals) in providing recommendations based on an organism's genetic profile. The genetic profiles and scores can also be used by ranchers, herders, corporations, veterinarians, animal reproduction specialists, trainers, owners, potential owners, fitness instructors, athletic coaches, therapists, chiropractors, acupuncturists, weight loss specialists, nutritionists, and the like in providing recommendations to an organism. Fitness instructors, athletic coaches, chiropractors, acupuncturists, weight loss specialists, nutritionists, therapists, psychologists, behaviorists, and the like, can also consult with physicians and medical specialists in providing recommendations to an organism. The recommendations may aid in reducing the overall risk or predisposition to harmful or unwanted phenotypes, or in increasing the risk or predisposition to beneficial or wanted phenotypes. Recommendations may also be for increasing compatibility in relationships, mate selection for increased success or compatibility in relationships or in childbearing decisions, mate pairing to produce offspring with a greater likelihood of desired phenotypes or a decreased likelihood of undesirable phenotypes or both, and others.

[00133] The genetic profile for an organism can have information on one or more specific phenotypes. Examples of other numbers of phenotypes included in a genetic profile are described herein. In some cases, a genetic profile can have a "score" that indicates a general risk or predisposition to the specific phenotype or to a group of phenotypes. The specific phenotype can be monogenic or multigenic (polygenic). The phenotype can also be multifactorial.

[00134] The phenotypes/conditions analyzed may include clinical and non-clinical phenotypes. Phenotypes/conditions can include medical conditions such as diseases and disorders, e.g., described herein. Phenotypes can also include specific traits. Specific traits may include physical traits, physiological traits, mental traits, personality and emotional traits, breed, lineage (e.g., an organism's place of origin and organism's ancestor's place of origin), age (e.g., age expectancy, or age of onset, of different phenotypes, such as conditions and traits), and any other phenotype, such as diseases, disorders, or traits.

[00135] Some phenotypes concern an age of onset. “Age of Onset” may refer to the age that the phenotype is most likely to manifest or the age at which symptoms will first become noticeable and therefore the disease may be diagnosed.

[00136] In some embodiments, the genetic profile includes a score that indicates a risk or predisposition of an organism for one or more multifactorial phenotypes. The multifactorial inheritance of a phenotype is based on the interaction between genes and the environment. The genetic factors may be a number of genes; a number of genetic variants within the same or different genes or elsewhere within the genome that is not within a gene; the non-genetic factors may be environmental exposures; habits; or specific traits. Other factors that may also be included in the risk analysis of multifactorial phenotypes include abnormal or suggestive results from a medical examination or test; physical or mental symptoms; specific medical condition or medical history; family history or other genetic or non-genetic factor.

[00137] As described herein and as shown in **FIG. 24**, phenotypes may be monogenic, polygenic or multifactorial. **FIG. 24** shows that for a multifactorial phenotype, the total risk is composed of genetic and non-genetic factors, also referred to as environmental factors. The amount that genetics or the environment contributes to this risk differs by phenotype. For example, one phenotype may be determined by approximately 70% genetics and approximately 30% environment while another phenotype may be determined by approximately 40% genetics and approximately 60% environment. The amount that genetics contributes to a phenotype is called the phenotype’s heritability. Heritability for a specific phenotype may be determined from various scientific studies, such as twin studies or parent-offspring regression, and the heritability of specific phenotypes can be found in published scientific literature, such as journal articles.

[00138] An organism’s risk or predisposition for polygenic or multifactorial phenotypes can be calculated based on the allele or genotypes for one or more genetic variants associated with polygenic or multifactorial phenotype(s).

[00139] By determining genetic risk or predisposition for multifactorial phenotypes, one can identify those organisms at higher risk due to their genetics and then proactively adjust their modifiable risk due to one or more non-genetic factors, for example, by modifying , modifying medications, conducting screening exams, and instituting other or living changes. This approach can empower organisms, physicians, and health-care providers and enable them to identify non-genetic factors that can be modified and that will be of the most value. Although genetic risk may remain unchanged, decreasing risk due to non-genetic factors risk may have the effect of decreasing risk overall, thereby decreasing the incidence of that phenotype, delaying its onset, or decreasing its morbidity or mortality.

[00140] Similarly, the genetic basis for hundreds of monogenic phenotypes, such as diseases, have been known for years, but widespread screening for organisms carrying or affected by these phenotypes has never before been technologically feasible or cost-effective. By identifying organisms

who carry phenotype-related genetic variants, providers may offer extensive offspring planning options. Previously, there has not been such an 'early warning system' for such a large number of either monogenic and/or polygenic phenotypes.

[00141] In some embodiments, the caretakers of organisms are informed of the monogenic diseases that they carry and may pass on to future generations.

[00142] A genetic profile is determined by obtaining the genetic information of an organism and correlating the genetic information to a specific phenotype. A specific phenotype may be correlated to one or more genetic variants and their allele or genotype. Genetic markers and variants may include different numbers of nucleotide repeats, nucleotide insertions, nucleotide deletions, single nucleotide polymorphisms, multiple nucleotide length polymorphisms, chromosomal translocations, chromosomal duplications, length of telomeres, copy number variations, or any combination thereof. Copy number variation may include organism or multiple exons or other parts of a gene, an entire gene, multiple genes, microsatellite repeats, nucleotide repeats, centromeric repeats, or telomeric repeats.

[00143] Genetic markers and variants may also include epigenetic factors, such as methylation status. Genetic variants may also be changes to a single nucleotide, referred to as point mutations or polymorphisms or mutations or variants, such as single nucleotide polymorphisms, or SNPs. Genetic variants may also be changes to multiple nucleotides, such as changes to two or more nucleotides that are located next to each other or are not located next to each other. Genetic variants may also be the deletion or insertion of one or more nucleotides anywhere within an organism's genetic code, referred to as a deletion or insertion, or deletion insertion polymorphisms, or DIPs (also referred to as indels). Genetic markers and variants may include changes to nuclear DNA, mitochondrial DNA, chloroplast DNA, cytoplasmic DNA, plasmid DNA, or combinations thereof. Genetic markers and variants may also occur in genetic sequences that are not contained within a cell, such as from lysed cells at a crime scene or if genetic sequences are detectable in the blood or plasma, such as when fetal oligonucleotides exist within maternal blood. At times, genetic sequences, such as DNA or RNA or cells containing DNA or RNA, from one organism may occur within another organism and be able to be isolated or analyzed, such as when fetal cells can be detected and isolated from maternal blood during pregnancy, or such as with hematophagy when one organism, such as an insect, contains blood from another organism, such as within its stomach, and genetic analysis and a genetic profile can be determined from this source of genetic information as well. For non-human species, the genetic profile may be determined by obtaining genetic information from any source of genetic information, such as DNA or RNA, which may exist anywhere within the organism, such as within the cytoplasm of bacteria, within the nucleus and mitochondria of cells from mammals, within the capsid of viruses or within the nucleus and chloroplast of plants and eukaryotic algae.

[00144] Genetic variants may also be in linkage disequilibrium with other genetic variants that are detected or determined for an organism's genomic profile. Each new allele is typically initially

associated with the other alleles that happened to be present on the particular chromosomal background on which it arose. The specific set of alleles observed on a single chromosome, or part of a chromosome, is called a haplotype. New haplotypes can be formed by additional mutations or by recombination, such as between maternal and paternal chromosomes, resulting in a mosaic of the two parental haplotypes. The coinheritance of genetic variant alleles on these haplotypes leads to associations between these alleles in the population, known as linkage disequilibrium, LD. As the likelihood of recombination between two genetic variants typically increases with the distance between them, without being bound by theory, on average such associations between genetic variants decline with distance. In some cases, strong associations can mean that in many chromosome regions there are only a few haplotypes, which can account for most of the variation among organisms in those regions. In some embodiments, because of strong associations between genetic variants in a region, information about common genetic variants in a region can be determined through information for a few carefully chosen genetic variants in the region. As a result, only a few of these carefully chosen genetic variants can be used to identify each of the common haplotypes in a region. Linkage disequilibrium can be applicable to all types of genetic variants, including SNPs, DIPs, nucleotide repeats, translocations, methylation status, and CNVs, and is also applicable to all species, including humans and non-humans.

[00145] The genetic variants described herein may be used to determine specific haplotypes or diplotypes. For example, genetic markers or variants, such as SNPs, nucleotide repeats, insertions, deletions and other as described herein, may be in linkage disequilibrium with genetic markers that have been shown to be associated with specific phenotypes. For example, a nucleotide insertion is correlated with a phenotype and a SNP is in linkage disequilibrium with the nucleotide insertion. Through linkage disequilibrium, a disease predisposing allele cosegregates with a particular allele of a SNP or a combination of particular alleles of SNPs. A particular combination of SNP alleles along a chromosome is termed a haplotype, and the DNA region in which they occur in combination can be referred to as a haplotype block. While a haplotype block can consist of one SNP, typically a haplotype block represents a contiguous series of 2 or more SNPs exhibiting low haplotype diversity across organisms and with generally low recombination frequencies. An identification of a haplotype can be made by identification of one or more SNPs that lie in a haplotype block.

[00146] Databases of genetic variants are publicly available from, for example, the International HapMap Project (see www.hapmap.org, *The International HapMap Consortium, Nature* 426:789-796 (2003), and *The International HapMap Consortium, Nature* 437:1299-1320 (2005)), the United States National Institutes of Health's National Center of Biotechnology Information's Single Nucleotide Polymorphism database (dbSNP) (see www.ncbi.nlm.nih.gov/SNP/), the United States National Institutes of Health's National Center of Biotechnology Information's Entrez Global Query Cross-Database Search System (see [/www.ncbi.nlm.nih.gov/sites/gquery](http://www.ncbi.nlm.nih.gov/sites/gquery)) and the European Bioinformatics Institute and the Wellcome Trust Sanger Institute's Ensembl project (see www.ensembl.org/).. These

databases provide information on genetic variants and genetic variants in linkage disequilibrium patterns. Thus, linkage disequilibrium data can be ascertained through the data publically available from the International HapMap Project.

[00147] Linkage disequilibrium (LD) can be measured by the variables D and r^2 , such as described by Hill and Robertson (*TAG Theoretical and Applied Genetics* **38**: 226-231 (1968)). The International HapMap provides these measures of LD for genetic variants. For example, r^2 is a measure of the LD between two genetic variants and the range of r^2 is from zero to one. Thus, in embodiments using such a system of measure, genetic variants that have greater r^2 values tend to segregate together, such that two genetic variants that have an $r^2=1$ always appear together.

[00148] For some genetic variants that are found to be associated with a phenotype, the specific genetic variant is the cause of that phenotype (that genetic variant is the causal genetic variant). For example, on chromosome 1 in the coagulation factor V gene (F5), there exists a genetic variation (an adenine base appears instead of a guanine, IUPAC nucleotide code R (see **Table 1**)) that changes amino acid position 506 from an Arginine (Arg) to a Glutamine (Gln) (see **Table 2** for IUPAC amino acid codes used herein), which appear in dbSNP as rs6025 (*Bertina et al., Nature* 369:64-67 (1994)). This genetic variant (called Factor V Leiden) was found to be one of the direct causes of activated protein C resistance, which causes the thrombophilia phenotype. Without being bound by theory, it is thought that any genetic variant that is in tight LD (has a high r^2 value) with the Factor V Leiden genetic variant may also be associated with thrombophilia.

[00149] The sequence for a genetic variant may be from any available database, public or private. For example, the sequence data may be from the March 2006 human reference sequence (NCBI Build 36.1), produced by the International Human Genome Sequencing Consortium and the mitochondrial sequence may be from NCBI Genebank #AC_000021.2. For cow, the sequence data may be from the October 2007 Bos Taurus draft assembly (Baylor release Btau_4.0), produced by the Baylor College of Medicine Human Genome Sequencing Center. For chicken, the sequence data may be from the May 2006 chicken (Gallus gallus) v2.1 draft assembly, produced by the Genome Sequencing Center at the Washington University School of Medicine in St. Louis, MO, USA (WUSTL). For dog, the sequence data may be from the May 2005 dog (Canis familiaris) whole genome shotgun (WGS) assembly v2.0, sequenced and assembled by the Broad Institute of MIT/Harvard and Agencourt Bioscience. For horse, the sequence data may be from the Sep. 2007 Equus caballus draft assembly EquCab2 (UCSC version equCab2), produced by The Broad Institute. For pig, sheep, goat, turkey, and any other organism that does not yet have a draft assembly or full genome sequence available at this time the sequence data may be from journal articles that discuss a specific genetic variant and/or the genetic sequence surrounding and/or including the genetic variant. For cat, the sequence data may be from the March 2006 Felis catus draft assembly (Broad Release 3), produced by the Broad Institute of MIT/Harvard and Agencourt Bioscience. For chimpanzee, the sequence data may be from the March 2006 chimpanzee (Pan troglodytes) browser displays data from the 6X whole genome shotgun

draft assembly (Build 2 Version 1, Oct. 2005), produced by the Chimpanzee Sequencing and Analysis Consortium. For mouse, the sequence data may be from the July 2007 mouse (*Mus musculus*) genome data, obtained from the Build 37 assembly by NCBI and the Mouse Genome Sequencing Consortium. For rat, the sequence data may be from the November 2004 rat (*Rattus norvegicus*) genome assembly, based on version 3.4 produced by the Atlas group at Baylor Human Genome Sequencing Center (HGSC) as part of the Rat Genome Sequencing Consortium. For platypus, the sequence data may be from the v5.0.1 *Ornithorhynchus anatinus* draft assembly, produced by the Genome Sequencing Center at Washington University, St. Louis. For guinea pig, the sequence data may be from the Feb. 2008 *Cavia porcellus* draft assembly (Broad Institute cavPor3), produced by the Broad Institute at MIT and Harvard. For rhesus, the sequence data may be from the January 2006 rhesus macaque (*Macaca mulatta*) draft assembly v.1.0, Mmul_051212, obtained from the Baylor College of Medicine Human Genome Sequencing Center (BCM HGSC). For orangutan, the sequence data may be from the Jul. 2007 *Pongo pygmaeus abelii* draft assembly (WUSTL version Pongo_abelii-2.0.2), produced by the Genome Sequencing Center at Washington University School of Medicine in St. Louis (WUSTL). And for lizard, the sequence data may be from the Feb. 2007 *Anolis carolinensis* draft assembly (Broad Institute AnoCar (1.0)), produced by the Broad Institute at MIT and Harvard. For example, a human genetic variant for the F5 gene may be referenced as “F5 Chr. 1: 167785673 R”, meaning that the genetic variant exists within or bordering the F5 gene on chromosome 1, at position 167785673 on chromosome 1, and that the base is either an adenine or a guanine. The sequence numbering can be relative to the coordinate systems for each chromosome from NCBI Build 36.1. All coding and abbreviations are based on IUPAC nomenclature. The genomic sequence surrounding this genetic variant on the reverse strand is as follows, with R (A or G) appearing at position 167785673: TGTAAGAGCAGATCCCTGGACAGGC(R)AGGAATACAGGTATTTTGTCCCTGA

Table 1: IUPAC Nucleotide Codes

IUPAC Nucleotide Code	Base
A	Adenine
C	Cytosine
G	Guanine
T (or U)	Thymine (or Uracil)
R	A or G
Y	C or T
S	G or C
W	A or T
K	G or T
M	A or C
B	C or G or T
D	A or G or T
H	A or C or T
V	A or C or G
N	Any base

-	gap
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Table 2: IUPAC Amino Acid Codes

IUPAC Amino Acid Code	3 Letter Code	Amino Acid
A	Ala	Alanine
C	Cys	Cysteine
D	Asp	Aspartic Acid
E	Glu	Glutamic Acid
F	Phe	Phenylalanine
G	Gly	Glycine
H	His	Histidine
I	Ile	Isoleucine
K	Lys	Lysine
L	Leu	Leucine
M	Met	Methionine
N	Asn	Asparagine
P	Pro	Proline
Q	Gln	Glutamine
R	Arg	Arginine
S	Ser	Serine
T	Thr	Threonine
V	Val	Valine
W	Trp	Tryptophan
Y	Tyr	Tyrosine

[00150] Some associations between genetic variants and risk of disease are based upon a ‘signal’ of risk in the vicinity of that genetic variant. The genetic variant may not be the causal genetic variant (ie. it may not be the exact cause of the phenotype) but because it is in LD with the causal variant, the non-causal genetic variant shows an association with the phenotype. These signals can be used clinically as they can allow for the ascertainment of risk from signals (genetic variants in LD with the causal genetic variant) without the exact causal variant being specifically known at that moment. For example, as described in Zeggini et al. (*Nat. Genet.* 40: 638-645 (2008)), Zeggini et al. conducted a research study examining genetic variants associated with Diabetes Mellitus, Type II (DMII). They found that both rs2641348 and rs2934381 were associated with DMII, but based on data from the International HapMap Project, they wrote that SNPs rs10923931 and rs2641348 appear to represent the same signal ($r^2 = 0.92$ in HapMap CEU).

[00151] In another example, McCarroll et al. (*Nat Genet* 40:1107-1112 (2008)) conducted research on the cause of the association (the cause of the signal) that had previously been detected (*Parkes et al. Nat Genet* 39:830-832 (2007); *The Wellcome Trust Case Control Consortium Nature* 447:661-678 (2007); *Franke et al. Nat Genet* 40:713-715 (2008)) between region 5q33.1 (containing the IRGM gene) and Crohn’s disease (CD). McCarroll et al. found that a specific genetic variant in LD with previously reported genetic variants (rs13361189 and rs4958847) in the region may be the actual causal genetic variant in that region associated with a predisposition for Crohn disease. They found a common, 20-kb deletion polymorphism upstream of IRGM and in perfect linkage disequilibrium ($r^2 = 1.0$) with the most strongly CD-associated SNP, that causes IRGM to segregate in the population with

two distinct upstream sequences. As a result, their work identified a 20-kb deletion polymorphism as the likely causal variant. Thus, conducting genetic testing either for this deletion directly or for genetic variants rs13361189 or rs4958847 (or any other genetic variants in tight LD with the 20-kb deletion) is likely to give the same information about the same signal. Any one of these genetic variants in tight LD with each other can be used to ascertain a specific predisposition to Crohn's disease in relation to the signal at 5q33.1. As a result, any one of the genetic variants can be tested for, and used to discern whether an organism has a predisposition for Crohn disease based on the specific signal in this region (5q33.1, IRGM gene) of the genome.

[00152] Causal genetic variants, or genetic variants in LD with the causal genetic variants, are contemplated herein. For example, genetic variants detected for an organism may be in LD with a causal genetic variant. The genetic variants detected may have an r^2 value of at least 0.2, 0.4, 0.5, 0.6, 0.7, 0.75, 0.8, 0.85, 0.86, 0.87, 0.88, 0.89, 0.9, 0.91, 0.92, 0.93, 0.94, 0.95, 0.96, 0.97, 0.98, 0.99, or 1 with a causal genetic variant. In some embodiments, the genetic variants detected may have an r^2 value of at least 0.2, 0.4, 0.5, 0.6, 0.7, 0.75, 0.8, 0.85, 0.86, 0.87, 0.88, 0.89, 0.9, 0.91, 0.92, 0.93, 0.94, 0.95, 0.96, 0.97, 0.98, 0.99, or 1 with published genetic variants that are correlated or associated with a phenotype.

[00153] In another aspect of the present invention, methods of using oligonucleotides that specifically detect a genetic variant, either a genetic variant directly correlated with a condition, or a genetic variant in linkage disequilibrium with a genetic variant that is correlated to a phenotype. Preferably, the genetic variant detected by such an oligonucleotide is associated with a phenotype, such as a medical condition. The association of a genetic variant with a phenotype may be from a scientific publication. The genetic variant that is detected can also be correlated to a non-phenotype. In another aspect, other genetic variants, such as described herein, may be detected by oligonucleotides specifically selected to detect such genetic variants, wherein the genetic variants are correlated to a phenotype, such as medical conditions, non-medical conditions, or a combination thereof.

[00154] Genetic variants that are not available in public databases can also be used to generate an organism's genetic profile. Furthermore, sequences to detect genetic variants may be unique sequences (e.g., those not listed in public databases, such as NCBI's dbSNP Builds 126 - 129 for example) upstream or downstream (flanking) of a genetic variant. For example, the sequence may contain sequence information that encompasses about 10, 15, 20, 25, 30, 35, 40, 45, 50, 60, 75, 100, 150, or 200 bps or more immediately upstream or downstream of a genetic variant. The genetic profiles can be determined from oligonucleotide sequences wherein at least 5, 10, 25, 50, 65, 70, or 75% of the sequences corresponding to a genetic variant are sequences not listed in a public database, for example sequences about 20, 25, 30, 35, 40, 45, 50, 60, 75, 100, 150, or 200 bps or more (upstream or downstream) of the genetic variant. The sequences to detect genetic variants, or the sequence of a genetic variant, such as the deleted sequence of a deletion polymorphism, may be stored in a private database, such as, but not limited to, the Predictive Medicine Database further described

below, and illustrated in **Example 9**. The private database may be constructed to comprise both publicly available genetic variants, such as sequences containing these genetic variants from public databases as well as sequences not available in public databases. The private database may have at least about 50, 100, 1000, 5000, 6,000, 6,500, 7,000, 8,000, 10,000, 15,000, 20,000, 25,000, 30,000, 45,000, 50,000, 100,000, 150,000, 200,000, 250,000, 300,000, 350,000, 400,000, 450,000, 500,000, 750,000, 1,000,000, 1,500,000, 2,000,000, 2,500,000, 3,000,000, 3,500,000, 4,000,000, 4,500,000, 5,000,000, 5,500,000, 6,000,000, 6,500,000, 7,000,000, 7,500,000, 8,000,000, 8,500,000, 9,000,000, 9,500,000, 10,000,000 or more genetic variants, such as SNPs, that are associated with specific phenotypes, such as diseases or traits. The private database may contain genetic variants associated with specific phenotypes, such as diseases or traits, present in at least 100, 250, 500, 750, 1000, 1250, 1500, 2000, 3000, 3500, 4000, 4500, 5000, 5500, 6000, 6500, 7000, 7500, 8000, 8500, 9000, 9500, 10,000, 10,500, 11000, 11500, 12000, 12500, 13,000, 13,500, 14,000, 14,500, 15,000, 15,500, 16,000, 16,500, 17,000, 17,500, 18,000, 18500, 19000, 19500, or 20,000 genes.

[00155] The database may contain genetic variants present in non-coding regions. The genetic variants may be medically related or non-medically related. The genetic variants, such as SNPs, may include only clinically relevant genetic variants, or genetic variants in genes or in linkage disequilibrium with other genetic variants correlated with clinical phenotypes. The SNPs, or other genetic variants, may be organized by medical specialty, organ system, gene, chromosome, location on a chromosome, or phenotype. The SNPs, or other genetic variants, can be organized by clinical severity or by how well that genetic variant is thought to correlate with a specific phenotype or by the degree or status of replication of that genetic variant with its associated phenotype. The private database can also have precise information for each genetic variant, such as a SNP. For example, information such as odds ratio, relative risk, hazard ratio, absolute risk value, applicable populations and ethnicities/species, inheritance patterns, journal references, journal links, genetic variant synopsis, phenotype information, phenotype prevalence, phenotype incidence, genetic variant allele frequencies, and recommendations or interventions, such as those that have been associated with decreasing the incidence or impact of that phenotype.

[00156] In some embodiments, the database is a Predictive Medicine Database (PMD), which can be constructed from, or through a review of some, many, or all published studies throughout some, many, or all worldwide journal articles relating to specific genetic variants associated with a phenotype (disease, condition, trait, process, modifier of other phenotype, and others). The PMD can allow for a an analysis, a comprehensive analysis, or a complete analysis of some, many or all known phenotype-associated genetic variants throughout the partial or entire genome of an organism of any species. The PMD may or may not be part of an Analytical IT System (**FIG 1**). An Analytical IT System can process genetic data from genetic testing and/or may analyze genetic information from genetic testing. An Analytical IT System may also process non-genetic factors (such as medical history and/or primary location an animal may be raised, such as free-range or caged) and may

include that non-genetic information in the analysis of the genetic data and/or genetic information. An Analytical IT System may associate the genetic information or data with one or more phenotypes. The Analytical IT System may, or may not, include, be part of, or be able to access one or more phenotype matrices, gene matrices, and/or genetic variant matrices (described herein). The Analytical IT System may enable and make possible comprehensive, integrated and/or actionable genetic analysis and/or clinical genetic analysis and/or may enable partial genome analysis, full genome analysis (e.g., whole genome analysis), partial genome clinical analysis and/or full genome clinical analysis (e.g., whole genome clinical analysis).

[00157] One or more Analytical IT System(s) may be capable of analyzing genetic data and/or information, such as allele or genotype data for one or more genetic variants within a genome and may be capable of generating an analysis, such as a genetic report (described herein). In some embodiments, a number of PMDs are generated, wherein each PMD is specific for a particular species. For example, a PMD may be provided for humans, and another PMD for canines. The PMD can also be agnostic, in that the data in the PDM can be utilized on any genetic testing platform (such as those provided by Illumina, Sequenom, General Electric, Agilent, 454 Life Sciences, Pacific Biosciences, Complete Genomics, Helicos BioSciences, Intelligent Bio-Systems, IBM, ION Torrent Systems, Halcyon Molecular, GE Global, Stratos Genomics, Genome Corp., Genome Diagnostics, Agencourt Bioscience, Microchip Biotechnologies, or Affymetrix) and with any genetic testing methodology (such as arrays, massarrays, beadarrays, microarrays, genechips, PCR, partial or full exome sequencing, and partial or full genome sequencing, such as with pyrosequencing, nanopore, fluorophores, nanopore sequencing, nanoballs, sequencing by synthesis, sequencing by expansion, single molecule real time technology (SMRT)TM, true single molecule sequencing technology (tSMS)TM, or sequencing by ligation, microfluidics, infrared fluorescence, or other sequencing method or apparatus including others described herein) and with any genetic testing methodology (such as arrays, massarrays, beadarrays, microarrays, genechips, PCR, partial or full exome sequencing, and partial or full genome sequencing, such as with pyrosequencing, nanopore, fluorophores, nanopore sequencing, nanoballs, sequencing by synthesis, sequencing by ligation, or other sequencing method or apparatus including others described herein). Alternatively, the PMD can also be used only for one or more specific platforms. In some embodiments, all specific genetic variants associated with any discernible phenotype are included within the PMD, including single nucleotide polymorphisms (SNPs), deletion and insertion polymorphisms (DIPs), mutations, repeats, inversions, duplications, copy number variations (CNV), rearrangements, telomere size, and epigenetic factors such as methylation status. The genetic variants may be throughout the entire genome, including those that may exist within or near binding sites, such as transcription binding sites, translation binding sites, or microRNA (miRNA) binding sites, as well as genetic variants that may exist in DNA or RNA within the nucleus, mitochondria, freely within blood or plasma or in the cytoplasm. Genetic variants may

also be detected in genetic material that exists in any location in different species, such as contained within the capsid of a virus or within the nucleus or chloroplast of a plant.

[00158] The database may be constructed to contain variety of fields dependent upon the particular desired use, the genetic variants being analyzed or the types of scores being provided in the report to the client. Fields of the database are first created and all ascertainable data from each and every journal article is then entered into each of the fields. Nomenclature used in the database can follow the recommendations of The Ad Hoc Committee on Mutation Nomenclature (*Human Mutation* 8(3): 197-202); Beutler et al. (V. A. M. A. G. M. C. R. S. F. H. *Human Mutation* 8(3): 203-206 (1996)); Stylianou and Antonarakis (*Human Mutation* 11(1): 1-3 (1998)); and den Dunnen, S. E. A. (*Human Mutation* 15(1): 7-12 (2000)).

[00159] Journal articles can be divided by diseases and genetic variants that are monogenic or deterministic versus those that are polygenic or multifactorial and risk-associated.

[00160] The PMD fields may include: Full Gene Name or Locus (if the genetic variant is not located within or bordering a gene), Gene Symbol, Gene Locus, and Exact Genetic Variant Identification. The Exact Genetic Variant Identification can be the National Center for Biotechnology Information dbSNP rs identifier number (rs#) (see for example, www.ncbi.nlm.nih.gov/SNP/), along with the current NCBI Map to Genome Build number and the current NCBI build number for each rs# (such as www.ncbi.nlm.nih.gov/mapview/map_search.cgi?taxid=9606). Information about the gene name, symbols, and location and other pertinent information can be found from various NCBI databases, Entrez Pubmed (see for example, www.ncbi.nlm.nih.gov/sites/entrez), the Online Mendelian Inheritance in Man® (OMIM®) database (see for example, www.ncbi.nlm.nih.gov/sites/entrez?db=omim), the Online Inheritance in Animals (OMIA) database (see for example, www.ncbi.nlm.nih.gov/sites/entrez?db=omia) and also the European Bioinformatics Institute and the Wellcome Trust Sanger Institute's Ensembl project (see www.ensembl.org/). Journal articles can be from any journal from around the world that contains published studies of genetic variant-phenotype associations, and may be found through such resources as print version of the journal, libraries, and various internet resources such as through Entrez Pubmed (see for example, www.ncbi.nlm.nih.gov/sites/entrez).

[00161] Alternatively, the Exact Genetic Variant Identification can be the exact genomic sequence surrounding the genetic variant. For example, it can be the 25, 50, 100, or 200 bp of sequence upstream (5' flank) of the variant or 25, 50, 100, or 200 of sequence downstream (3' flank) of the variant or both. In some cases, the Exact Genetic Variant Identification can be about 4, 5, 8, 10, 15, 20, 25, 30, 35, 40, 45, or 50 bp of sequence upstream and downstream of the variant. Sources of sequence information can be any available in the arts, such as, but not limited to the Human Genome Project's Reference Sequence, Celera's Sequence, the European Molecular Biology Laboratory-European Bioinformatics Institute-Sanger Institute's Ensembl database (such as from www.ensembl.org/Homo_sapiens/index.html) and the National Center for Biotechnology Information

database (www.ncbi.nlm.nih.gov/gene). The genomic sequence surrounding the genetic variant can be identified according to International Union of Pure and Applied Chemistry (IUPAC) nucleotide ambiguity codes, as described by Cornish-Bowden (*"IUPAC-IUB SYMBOLS FOR NUCLEOTIDE NOMENCLATURE"* *Nucl. Acids Res.* 13: 3021-3030.) The genetic variant position on the chromosome relative to the coordinate system, as appears in the European Molecular Biology Laboratory-European Bioinformatics Institute-Sanger Institute's Ensembl database or Entrez Gene database of the National Center for Biotechnology Information's website can also be used, as well as identification of the strand direction of the sequences identified above. An unique internal identification number can also be assigned to each sequence, such as an "eg" number (the letters 'eg' followed by a unique number that can be between 1-20 digits long), to facilitate its identification.

[00162] Other PMD fields may include location of the genetic variant in or near the gene, such as Intergenic, Intron, Exon, Promoter, Regulatory, Enhancer, 3'untranslated region, 5'untranslated region, Intron Splice Site, Exon Splice Site, or miRNA Binding Site. For genetic variants that exist within or near genes, other PMD fields can include position within gene relative to start codon, amino acid number that the genetic variant occurs within, amino acid change that occurs due to genetic variant according to IUPAC nomenclature (*Nomenclature, I.-I. C. o. B. (1966). J. Biol. Chem.* 241(11): 2491-249.), and the function of change that occurs, for example, Nonsense, Missense, Sense, Synonymous, Nonsynonymous, Conservative, Non-conservative, Splicing Regulation (Domain Preserved or Abolished).

[00163] Other PMD fields may be Allele 1 (specific nucleotide if it is a SNP or nucleotide sequence if it is a DIP or repeat, or copy number if it is a CNV), Allele 2 (specific nucleotide if it is a SNP or nucleotide sequence if it is a DIP or repeat, or copy number if it is a CNV), Phenotype-associated Allele (Specific nucleotide if it is a SNP or nucleotide sequence if it is a DIP or repeat, or copy number if it is a CNV), or Phenotype-associated haplotype or diplotype for two or more genetic variants (if applicable), and Phenotype-associated Genotype (Specific genotype if it is a SNP or nucleotide sequence if it is a DIP or repeat, or copy number if it is a CNV). The haplotype for two or more genetic variants may have all genetic variants and their allele or genotype within the haplotype clearly annotated along with the Phenotype-associated haplotype or diplotype.

[00164] Genetic effect and risk prediction algorithm assessment (see for example, *Tabor et al. (2002). Nat Rev Genet* 3(5): 391-397) can also be a PMD field. Under this field, genetic effect and risk prediction algorithms utilizing one or more from the following may be listed:

[00165] A) PupaSuite (*Conde et al. (2006). Nucl. Acids Res.* 34(suppl_2): W621-625; *Reumers et al. (2008). Nucl. Acids Res.* 36(suppl_1): D825-829; *Yang and Nielsen (2002). Mol Biol Evol* 19(6): 908-917), such as PMut (*Ferrer-Costa et al. (2005). Bioinformatics* 21(14): 3176-3178), Phylogenetic Analysis by Maximum Likelihood (PAML) (*Yang. (2007). Mol Biol Evol* 24(8): 1586-1591), and/or SNPeffect (*Reumers et al. (2006). Bioinformatics* 22(17): 2183-2185; *Dantzer et al. (2005). Nucl. Acids Res.* 33(suppl_2): W311-314);

[00166]B) MutDB (Dantzer et al. (2005). *Nucl. Acids Res.* 33(suppl_2): W311-314), such as Sorting Intolerant From Tolerant (SIFT) (Ng and Henikoff (2003). *Nucl. Acids Res.* 31(13): 3812-3814) and/or Swiss-Prot (Bairoch and Boeckmann B (1991). *Nucleic Acids Res* 19:2247);

[00167]C) FastSNP (Yuan et al. (2006). *Nucl. Acids Res.* 34(suppl_2): W635-641), such as Polymorphism Phenotyping (PolyPhen)(Sunyaev et al. (2001). *Hum. Mol. Genet.* 10(6): 591-597; Sunyaev et al. (2000). *Trends in Genetics* 16(5): 198-200; Ramensky et al. (2002). *Nucl. Acids Res.* 30(17): 3894-3900), Transcriptional Factor Search (TFSearch)(Heinemeyer et al. (1998). *Nucl. Acids Res.* 26(1): 362-367; Akiyama: "TFSEARCH: Searching Transcription Factor Binding Sites", www.rwcp.or.jp/papia/), Exonic Splicing Enhancers Finder (ESEfinder) (Cartegni et al. (2003). *Nucl. Acids Res.* 31(13): 3568-3571; Smith et al. (2006). *Hum. Mol. Genet.* 15(16): 2490-2508), RESCUE-ESE(Fairbrother et al. (2002). *Science* 297(5583): 1007-1013; Yeo et al. (2004). *Proc. Natl Acad Sci. USA* 101(44): 15700-15705), FAS-ESE (Wang et al. (2004). *Cell* 119(6): 831-845), and/or Swiss-Prot;

[00168]D) SNPs3D (Yue et al. (2006). *BMC Bioinformatics* 7(1): 166; Yue and Moulton (2006). *Journal of Molecular Biology* 356(5): 1263-1274; Zhen Wang. (2001). *Human Mutation* 17(4): 263-270); such as the Stability Model & Profile Model(Yue et al. (2005). *Journal of Molecular Biology* 353(2): 459-473; Yue and Moulton (2006). *Journal of Molecular Biology* 356(5): 1263-1274);

[00169]E) VisualSNP (genepipe.ibms.sinica.edu.tw/visualsnp/input.do); and/or

[00170]F) FANS (fans.ngc.sinica.edu.tw/fans/input.do), which is typically used for unique sequences, i.e. those without dbSNP rs numbers. (C.K. Liu, Y.H. Chen, C.Y. Tang, S.C. Chang, Y.J. Lin, M.F. Tsai, Y.T. Chen and Adam Yao (2008) Functional analysis of novel SNPs and mutations in human and mouse genomes, *BMC Bioinformatics*, 9(Suppl 12)).

[00171]For genetic variants that predispose to a phenotype, such as for multifactorial phenotypes, other PMD fields may include one or more of the following: Risk Value, Risk Type (Odds Ratio, Relative Risk, or Hazard Ratio), Confidence Interval for risk value, p-value of risk value or cumulative or absolute value, Cumulative or Absolute Value (such as an Absolute Value, Absolute Risk or Lifetime Risk); Cumulative or Absolute Value Descriptor; Minor Allele Frequency (MAF) or Haplotype Frequency; Specific Population(s) that the risk and risk-allele (or risk-genotype or risk-haplotype) applies to, incidence of non-phenotype associated allele or genotype in disease cohort, incidence of phenotype associated allele or genotype in control cohort; total number of that specific population within the disease cohort(s); total number of that specific population within the control cohort(s); inheritance (such as Autosomal Recessive, Autosomal Dominant, Multiplicative, Additive, X-linked Recessive, X-linked Dominant, and others); Study Type (such as: Prospective, Retrospective, Genome-wide Association Study, Case-Controlled, and others); and various rating system (as described below) information, such as Replication Status of the genetic variant-phenotype association; Genetic Variant-Phenotype Score Rating (GVP Score); Genetic Variant-Phenotype

Triage (GVP Triage) also referred to as the Genetic Variant-Phenotype's Clinical Significance Rating (CSR), and/or SNP Rank.

[00172] For genetic variants that are deterministic of a phenotype, such as for monogenic phenotypes, PMD fields may include one or more of the following: Inheritance (such as Autosomal Recessive, Autosomal Dominant, Codominance, Incomplete Dominance, X-linked Recessive, X-linked Dominant, etc.), Replication Status, Genetic Variant-Phenotype Score Rating (GVP Score), Genetic Variant-Phenotype Triage (GVP Triage) also referred to as the Genetic Variant-Phenotype's Clinical Significance Rating (CSR), and/or Study Type (such as: Prospective, Retrospective, Genome-wide Association Study, etc.).

[00173] Other PMD fields may include, but not be limited to, Journal Article Author's Name(s), Journal Article's Date of Publication, Name of Journal, Primary Journal Article Reference, World Wide Web (www) address of the pubmed listing of the journal article, World Wide Web (www) address of the actual journal article, and/or References of any other published study on that specific genetic variant-phenotype association. Haplotypes may also be included in the PMD, and each haplotype-phenotype-risk value association may receive its own unique haplotype identifier number. All genetic variants that compose the haplotype may be listed in the PMD, as shown in the fields below. The specific haplotype under its unique identified number can list the genetic variants that compose the haplotype along with the genetic variant's alleles or genotypes that compose the haplotype and are associated with the risk-value for that specific phenotype in that specific population. Selected PMD fields are shown in **Table 3**.

Table 3: Database Categories or Fields

Fields
Type of Study
Exact Journal Article Reference
World Wide Web (www) address for actual article or pubmed listing of the article
Journal Article's Author's Name(s)
Journal Article's Date of Publication
Name of Journal
Institute, Medical Center, or Collaboration that Conducted the Study
What Country or Countries was the Study Conducted Within
References to other Relevant Journal Articles of the Genetic Variant-Phenotype Association
Replication Status
Synopsis & Summation of Journal Article Relevant Results & Information
Gene Name
Gene Symbol(s)
Genetic Variant (dbSNP rs# or internal identifier, such as eg#)
Genetic Sequence (such as 50bp immediately upstream & downstream of genetic variant if no rs# available)
Chromosome & Locus
Exact Location on Chromosome (such as Ensembl's Coordinate System)
Amino Acid (AA) Change
Location in Gene (such as AA number) or distance from transcription start site
Strand Direction

Allele 1
Allele 2
Allele 3 (if applicable)
Allele 4 (if applicable)
MAF
Prediction of Effect of Genetic Variant Algorithm Value(s)
GVP Rank
GVP Score
GVP Triage
Phenotype
Phenotype-associated Allele(s)
Phenotype-associated Genotype(s)
Inheritance Pattern (Such as Autosomal Rec., Autosomal Dom., X-linked Rec., Multiplicative, etc.)
Risk Value (For phenotype-associated allele or phenotype-associated genotype)
Risk Type (OR, RR, or Z)
Confidence Interval for Rick Value
p-value for Rick Value
Cumulative Value/Absolute Value/Other Value
Cumulative or Absolute Value Descriptor
Genotype or Allele Associated with Phenotype & Risk Value
Incidence of phenotype associated allele in non-phenotype cohort
Incidence of non-phenotype associated allele in phenotype cohort
Specific Population(s)
Total Aggregate Disease Cohort Study Size(s)
Total Aggregate Control Cohort Study Size(s)
Is this Genetic Variant Part of a Haplotype? (If Yes, reference its Unique Haplotype Identifier Number)
If Part of Haplotype, List Exactly all of Other Genetic Variants in Haplotype
If Part of Haplotype, List Risk-associated Haplotype (alleles) or Diplotype (genotypes)
If Part of Haplotype, Haplotype Risk Value
If Part of Haplotype, Risk Type (OR, RR, or Z)
If Part of Haplotype, Confidence Interval for Rick Value
If Part of Haplotype, p-value for Rick Value
If Part of Haplotype, Cumulative Value/Absolute Value/Other Value
If Part of Haplotype, Specific Population(s)
If Part of Haplotype, Total Aggregate Disease Cohort Study Size(s)
If part of Haplotype, Haplotype Frequency in Population
If Part of Haplotype, Incidence of phenotype-associated haplotype or diplotype in non-phenotype cohort
If Part of Haplotype, Incidence of non-phenotype associated haplotype or diplotype in phenotype cohort

[00174] The information for PMD fields may be publicly available, such as through published journal articles, published studies, websites, or from databases such as the aforementioned Entrez Gene database or other Entrez databases, the Ensembl database, the National Center for Biotechnology Information dbSNP database, or the International HapMap Project.

[00175] The risks can represent an estimate for an organism to be at risk for, to have, to be a carrier of, or be predisposed to have, a phenotype (e.g., condition, disorder, disease, trait, and the like). The risks or predispositions may be indicated by a numerical value, such as a risk value. The risk value can be an odds ratio (OR), relative risk (RR), hazard ratio (Z), cumulative risk (CR), absolute risk

(AR), or lifetime risk (LR). The risk value, or degree of risk, can be expressed in numbers, words, colors, graphs, charts, pictures, or other means, for example, the risk value can be described as high, medium, low, or none. The risk value, or degree of risk, can also be expressed as a range, such as a range of numbers, for example, from -5 to +5, wherein -5 indicates a highly unlikely occurrence of a condition in an organism to +5, wherein there is a highly likely occurrence of a condition in an organism. The risk value, or degree of risk, can also be expressed in a range of colors, for example, red indicating a high risk of having a condition, yellow for no risk, and blue for a decreased risk (protection against) having a phenotype, such as a condition. The number or color ranges can also include numbers or ranges that indicate an organism's genetic profile shows a protective effect for the phenotype, such as a condition. The risk value, or degree of risk, can also be an absolute value (e.g., amount of milk production per day in kilograms). Further methods of calculating the risk of, carrier status of, or predisposition of an organism for a phenotype are provided herein. Such risks, predispositions and carrier statuses are also further described herein.

[00176] The score for a disease or condition can be determined by one or more genetic variants, such as polymorphisms, as well as other factors, such as non-genetic factors, including non-genetic factors or previously known diseases, conditions or traits. One or more scores can be generated for a genetic profile of an organism. An organism's genetic profile can include values or scores for one or more phenotypes, such as diseases or traits. A genetic profile can also include information for selected phenotypes, such as traits or conditions, such as only clinical conditions. Alternatively, a genetic profile can contain information for non-clinical phenotypes only, or a combination of clinical and non-clinical phenotypes. In some cases, an organism has a clinical genetic profile that includes at least 2, 3, 5, 10, 20, 50, 100, 150, 200, 500, or 1000 clinically-relevant phenotypes, such as conditions, diseases or disorders. In some cases, an organism has a clinical genetic profile that includes other numbers of phenotypes, as described herein. A non-limiting example of representative genes and loci included in the present invention is shown in **Table 4**.

Table 4: Representative Genes and Loci

Species	Primary	Alternative	Full Gene Name
	Gene / Locus Abbreviation	Gene Abbreviation(s)	
cow	CAPN3		calpain 3
cow	CAPN		μ-calpain
cow	DGAT1		acyl-CoA:diacylglycerol acyltransferase
cow	ARIH1		ariadne homolog, ubiquitin-conjugating enzyme E2 binding protein, 1
cow	BNBD-4		Beta4-defensin
cow	b-LG		b-lactoglobulin
cow	BoLA-DRB3		major histocompatibility complex, class II, DRB3
cow	BRUNOL6		bruno-like 6, RNA binding protein
cow	CAST		calpastatin

cow	CPT1C		carnitine palmitoyltransferase 1C
cow	CARD15	NOD2	Caspase Recruitment Domain 15
cow	CCL2	SCYA2	CCL2 chemokine (C-C motif) ligand 2
cow	CD14		CD14 molecule
cow	CCL3	CCL3L1	chemokine (C-C motif) ligand 3
cow	CXCL10		chemokine (C-X-C motif) ligand 10
cow	DGAT1		diacylglycerol O-acyltransferase homolog 1
cow	EDG1	S1PR1	endothelial differentiation sphingolipid G-protein-coupled receptor 1
cow	FASN		fatty acid synthase
cow	GHR		growth hormone receptor
cow	HEXA		hexosaminidase A (alpha polypeptide)
cow	IGF1		insulin-like growth factor 1
cow	IGF2		insulin-like growth factor receptor 2
cow	IFNG		interferon, gamma
cow	CXCR1	IL8RA	interleukin 8 receptor, alpha
cow	CSN3		kappa-casein
cow	LEP		leptin
cow	LEPR	Ob-R; Ob-RM	Leptin Receptor
cow			locus, chr10:96,040,448
cow			locus, chr2:130,846,723
cow			locus, chr20:45,114,461
cow			locus, chr20:53,350,405
cow			locus, chr29:44,373,740
cow			locus, chr5:84,279,557
cow	NPY		neuropeptide Y
cow	NALP7		NLR family, pyrin domain containing 7
cow	LXRA	NR1H3	nuclear receptor subfamily 1, group H, member 3
cow	SPP1	OPN	phosphoprotein 1
cow	bPl	CSH1	placental lactogen
cow	PARP6		polymerase family, member 6
cow	POU1F1		POU class 1 homeobox 1
cow	PMCH		pro-melanin-concentrating hormone
cow	RDH13		retinol dehydrogenase 13 (all-trans/9-cis)
cow	STAT5A	STAT5A; STAT5A/MGF	signal transducer and activator of transcription 5A
cow	SYT5		synaptotagmin V
cow	TG		thyroglobulin
cow	TLR4		Toll-like receptor 4
cow	TNNT1		troponin T type 1 (skeletal, slow)
cow	TNF	TNFa	tumor necrosis factor (TNF superfamily, member 2)
cow	UCP2	MGC127535	uncoupling protein 2
cow	UCP3		uncoupling protein 3
cat	p53		p53
cat	TYR		tyrosinase

chicken	CAPN3	p94	calpain 3
chicken	IGF1R		insulin-like growth factor 1 receptor
chicken	FAS		factor-associated suicide
chicken	VIPR-1		Vasoactive intestinal peptide receptor-1
chicken	GHR	GHBP	growth hormone receptor
chicken	GHSR		growth hormone secretagogue receptor
chicken	INS		insulin
chicken	MSTN	GDF8	Myostatin
dog	ALB		serum albumin
dog	OR52N9		olfactory receptor family 52 subfamily N-like
dog	NHEJ1		nonhomologous end-joining factor 1
dog	MLPH	MGC2771, MGC59733, SLAC2-A	melanophilin
dog	IGF1		insulin-like growth factor 1
dog	MITF		MITF microphthalmia-associated transcription factor
dog	CYP1A2		cytochrome P450 1A2
dog	DNM1		dynamitin 1
dog	MSTN	GDF8 GDF-8	myostatin
dog	CBD103		beta-defensin 103
dog	MC1R		melanocortin 1 receptor (alpha melanocyte stimulating hormone receptor)
dog	TYRP1		tyrosinase-related protein 1
horse	SILV	PMEL17	melanocyte protein 17 precursor
horse	AOAH	LOC100055508	acyloxyacyl hydrolase
horse	DRD4	LOC100147552	dopamine D4 receptor
horse	CRISP3	HSP-3	cysteine-rich secretory protein 3
horse	MC1R	MSH-R	melanocyte-stimulating hormone receptor
horse	SPATA1		spermatogenesis associated 1
horse	SLC36A1		solute carrier family 36 (proton/amino acid symporter), member 1
horse	KIT		v-kit Hardy-Zuckerman 4 feline sarcoma viral oncogene homolog
pig	DECR1		2,4-dienoyl CoA reductase 1, mitochondrial
pig	ADIPOR1		adiponectin receptor 1
pig	ADIPOR2		adiponectin receptor 2
pig	ADIPOQ	ADN; APM1; ACRP30	adiponectin, C1Q and collagen domain containing
pig	CCKAR		cholecystokinin type A receptor
pig	CART	CARTPT	cocaine- and amphetamine-regulated transcript
pig	CYB5A		cytochrome b5 type A (microsomal)
pig	DLX5		distal-less homeobox 5
pig	ESR1	ER-alpha	estrogen receptor 1
pig	IGFBP2		insulin-like growth factor binding protein 2
pig	IGFBP-3		insulin-like growth factor binding protein 3

pig	MAN2B2		mannosidase, alpha, class 2B, member 2
pig	MMP-2		matrix metalloproteinase-2
pig	MUC13		mucin 13
pig	MUC4		mucin 4, cell surface associated
pig	TRX		thioredoxin
pig	TXNIP		thioredoxin interacting protein
pig	TFRC		transferrin receptor
pig			zinc finger protein 7
pig	CTSB		cathepsin B
sheep	PRL		prolactin
sheep	DGAT1		diacylglycerol O-acyltransferase homolog 1
sheep	ABCG2		ATP-binding cassette, sub-family G (WHITE), member 2
sheep	GDF8		myostatin
sheep	MC1R		melanocortin 1 receptor
rhesus macaque	CRH		corticotropin releasing hormone

[00177] The genetic profile (e.g., analysis) can be determined from detecting at least approximately 2, 3, 4, 5, 10, 25, 50, 100, 1000, 2,000, 5000, 6,000, 6,500, 7,000, 8,000, 10,000, 12,000, or 15,000 genetic variants. In some cases,, genetic profiles can be determined from at least approximately 20,000, 25,000, 30,000, 45,000, or 50,000 genetic variants. The genetic variants may be correlated to a phenotype, such as medically relevant or non-medically relevant phenotypes or conditions. For example, a number of genetic variants (e.g., at least 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25, 30, 35, 40, 50, 60, 75, or 100) may cause, be associated with, or be correlated to a single phenotype, or a single genetic variant can be correlated to a single phenotype. A number of genetic variants may also be correlated to a number of phenotypes. Alternatively a single genetic variant may be associated with a number of phenotypes. Each genetic variant can be correlated or associated with at least one phenotype and each phenotype is correlated or associated with at least one genetic variant. For example, a genetic profile may be used to detect (or calculate the risk of , carrier status of , or predisposition for) at least 1, at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 20, at least 25, at least 30, at least 40, at least 50, at least 60, at least 70, at least 100, at least 200, or at least 500 phenotypes (e.g., phenotypes described herein). In some cases, a genetic profile is used to detect at least 2 phenotypes, but no more than 10 phenotypes, no more than 15 phenotypes, no more than 20 phenotypes, no more than 25 phenotypes, no more than 30 phenotypes, no more than 35 phenotypes, no more than 40 phenotypes, no more than 45 phenotypes, no more than 50 phenotypes, no more than 100 phenotypes, no more than 200 phenotypes, no more than 300 phenotypes, no more than 500 phenotypes, no more than 1000 phenotypes, or no more than about 10, about 20, about 50, about 100, about 200, about 300, about 500, or about 1000 phenotypes (e.g., phenotypes described herein). In some cases, a genetic profile is used to detect at least 3 phenotypes, but no more than 10 phenotypes,

no more than 20 phenotypes, no more than 50 phenotypes, no more than 100 phenotypes, no more than 200 phenotypes, no more than 300 phenotypes, no more than 500 phenotypes, no more than 1000 phenotypes, or no more than about 10, about 20, about 50, about 100, about 200, about 300, about 500, or about 1000 phenotypes (e.g., phenotypes described herein). In some cases, a genetic profile is used to detect at least 4 phenotypes, but no more than 10 phenotypes, no more than 20 phenotypes, no more than 50 phenotypes, no more than 100 phenotypes, no more than 200 phenotypes, no more than 300 phenotypes, no more than 500 phenotypes, no more than 1000 phenotypes, or no more than about 10, about 20, about 50, about 100, about 200, about 300, about 500, or about 1000 phenotypes (e.g., phenotypes described herein). In some cases, a genetic profile is used to detect at least 5 phenotypes, but no more than 10 phenotypes, no more than 20 phenotypes, no more than 50 phenotypes, no more than 100 phenotypes, no more than 200 phenotypes, no more than 300 phenotypes, no more than 500 phenotypes, no more than 1000 phenotypes, or no more than about 10, about 20, about 50, about 100, about 200, about 300, about 500, or about 1000 phenotypes (e.g., phenotypes described herein). In some cases, a genetic profile is used to detect at least 6 phenotypes, but no more than 10 phenotypes, no more than 20 phenotypes, no more than 50 phenotypes, no more than 100 phenotypes, no more than 200 phenotypes, no more than 300 phenotypes, no more than 500 phenotypes, no more than 1000 phenotypes, or no more than about 10, about 20, about 50, about 100, about 200, about 300, about 500, or about 1000 phenotypes (e.g., phenotypes described herein). In some cases, a genetic profile is used to detect at least 7 phenotypes, but no more than 10 phenotypes, no more than 20 phenotypes, no more than 50 phenotypes, no more than 100 phenotypes, no more than 200 phenotypes, no more than 300 phenotypes, no more than 500 phenotypes, no more than 1000 phenotypes, or no more than about 10, about 20, about 50, about 100, about 200, about 300, about 500, or about 1000 phenotypes (e.g., phenotypes described herein).

[00178] The genetic profiles can also be determined from detecting genetic variants in at least approximately 2, 5, 10, 25, 50, 100, 250, 500, 750, 1000, 1250, 1500, 2000, 2500, 3000, 3500, 4000, 5000, 6000, or genes or loci. In some embodiments, at least approximately 1000, 1500, 2000, 2500, 3000, 4000, 5000 genetic variants are detected in an organism's genetic profile. In some embodiments, approximately 50 or more, 100 or more, 200 or more, 500 or more, 1000 or more, 1500 or more, 2000 or more, 2500 or more, 3000 or more, 4000 or more, 5000 or more, or 6000 or more genetic variants are detected in an organism's genetic profile. In some embodiments, at least approximately 6000 genetic variants or at least approximately 6500 genetic variants are detected in an organism's genetic profile. The genetic profile can include genetic variant identification in at least 2, 5, 10, 25, 50, 100, 200, 500, 1000, 1200, 1500, 2000, 3000, 4000, 5000, or 6000 genes. In some embodiments, each of the genetic variants in the genes or loci are associated with one or more phenotypes. In some embodiments, each of the genetic variants in the genes or loci is medically relevant. In some embodiments, each of the sequences is linked to a journal reference or a preventive intervention/recommendation or both. In other embodiments, each of the genetic variants is for a

specific disease or for a specific type of genetic testing, such as for children, for adults, for newborns, for a fetus, for organisms that participate in sports or gambling activities, for carrier information, for research, for governmental agency purpose.

[00179] The genetic variants can also be used to determine the pharmacogenomic profile of an organism and be utilized in assessing clinical trials to stratify the population and further identify genetic variants associated with improved or decreased efficacy or adverse effects. For example, the genetic variants can be used to determine the suitability of a particular medication, drug or treatment for a given disease, condition or phenotype. For example, suitability may include determining whether an organism has a risk of reacting adversely to a drug or treatment, whether a drug may have little effect on the organism's condition (or phenotype), whether a drug is likely to be beneficial to the organism, whether one drug or treatment may be more effective or beneficial than another drug or treatment, whether the drug is likely to be effective in treating a condition, or the timeframe (such as described by a certain number of seconds, minutes, hours, days, weeks, months, years, or decades) in which a response, such as therapeutic response, is likely to be observed with a specific medication or class of medications. Suitability or pharmacogenomics results may include but are not limited to drug resistance, sensitivity, effectiveness, metabolism, absorption, or excretion of a specific drug or class of drugs such as for example aminoglycosides, anti-cancer drugs, sulfonamides, opiates or NSAIDs. Other pharmacogenomic results may include information on a suitable drug dosage for an organism, such as the most appropriate dose of a drug to start at in order to obtain effectiveness or increased effectiveness or to limit potential adverse effects, including but not limited to addiction, toxicity, allergic reaction, abuse potential, treatment-emergent suicidality, hypersensitivity, induced parkinsonism, resistance and intolerance. In some cases, genetic variants are "indicators of" or may be an indicator of which indicates that genetic testing and/or analysis can ascertain one of three possible phenotypes: an increased phenotype, a normal phenotype, or a decreased phenotype. In some cases, genetic variants may provide enhanced protection against an adverse phenotype given a specific intervention. For example, provided herein are variants that indicate hormone therapy may be particularly advantageous for protection against breast cancer.

[00180] Non limiting examples of pharmacogenomic genetic variants include variants in cytochrome P450 genes and any other genes involved in the pharmacodynamics, pharmacokinetics, metabolism, processing, excretion, and/or absorption of any injected, injected, absorbed, or inhaled substance.

[00181] The evaluation of the genetic variants and their relationship to phenotype and the significance to the client may be further analyzed to produce one of a variety of scores that combine two or more of the variants identified and in some embodiments also include non-genetic information about the client to provide a score as described herein. The particular profile or score provided in the report to the client to third party may be based on a request from the client, doctor or another third party as described herein.

[00182] The risk for a phenotype (e.g., specific disease, disorder, characteristic, trait or condition), including responses to drug treatments, such as efficacy of a drug, may be represented by a score or action score. For example, a score or action score for a specific disease or trait can be determined by multiplying the phenotype's Clinical Significance Rating (CSR), Phenotype Impact Rating (PIR) and Notice Me Factor (NMF). In other embodiments, an Action Score (AS) may be determined by using a subset of the aforementioned factors, additional factors, or a combination thereof, as further described below. Other scores or measures may also be determined (See for example, **FIG. 6, Table 8, Table 9A-9B and Example 7**).

[00183] The Generic Lifetime Risk (GLR) is the gender-specific or gender matched lifetime risk of a specific phenotype for a population and this can be obtained from published literature and various resources such as from the United States Department of Health and Human Services' Centers for Disease Control and Prevention (CDC) and National Institutes of Health (NIH). The GLR may also be age-matched and/or gender-matched for a population. The Cumulative Genetic Risk (CGR) is the organism's risk of a phenotype based on their genetic profile, containing one or more genetic variants associated with risk for that phenotype, and is determined by taking into account all relevant genetic variants associated with that phenotype. The Predictive Medicine Risk (PMR) is the organism's new lifetime risk for a phenotype based on the phenotype's GLR and the organism's CGR.

[00184] The PIR (also known as the DIR), or Phenotype Impact Rating, indicates the clinical severity of a phenotype. For example, the PIR ranges from -3 to +3, where -3 causes sudden death or debilitating phenotype, such as a disease, -2 indicates a serious phenotype, such as a disease, a phenotype, such as a disease or condition, that is difficult to cure, may cause death, or has significant negative life consequences, -1 indicates a phenotype, such as a disease or condition, that is usually manageable, 0 is a neutral phenotype, such as a condition or trait, +1 indicates a slightly positive phenotype, such as a condition or trait; +2 indicates that the phenotype is a helpful trait or protection against (lower risk of) a harmful phenotype, such as a condition, and +3 indicates a significant advantage or significant protection against a harmful phenotype, such as a condition.

[00185] The Genetic Variant-Phenotype Score (GVP score) may be used as a measure or rating system for genetic variant-phenotype correlations, or the association or strength of association between a genetic variant's allele or genotype and a phenotype, such as a disease or condition. For example, a GVP score can be determined for a disease or trait, such as milk production, based on studies correlating a genetic variant with a phenotype.

[00186] As the association between polygenic and multifactorial genetic variants and their phenotypes, such as diseases, disorders or traits, is complex, there may exist different levels of replication, validation, substantiation and confirmation that a genetic variant is associated with a specific phenotype, such as a disease, disorder or trait. For example, research (e.g., a clinical study) as to the association between genetic variant A and disease X may either be preliminary or may be highly substantiated or validated through studies in different cohorts that replicate similar results. An

organism may have different levels of associations between a genetic variant and a phenotype determined and reported. For example, an organism's genetic profile may be reported with different sections divided by the level of replication, substantiation, validation and confirmation (e.g., the level the associations have been replicated, substantiated, validated or confirmed). The report may have a first section that contains genetic variant-phenotype associations that are only highly replicated and substantiated while the second section contains phenotype information assessed from genetic variant-phenotype associations that are highly replicated and substantiated and also moderately replicated and substantiated, and so forth. For example, there may only be preliminary information about a genetic variant's association with toxicity for a medication used in kidney transplant recipients. A kidney transplant physician or researcher, such as a clinical trial researcher, may find this information useful in watching adverse reactions or in determining the starting dose of the medication even if the association is not substantiated by replicated studies.

[00187] Factors that can be used in a system for rating genetic variant alleles or genotypes and their correlations with one or more phenotypes may include, but are not be limited to, the aggregate number of organisms in the disease cohort(s), or cohort(s) exhibiting a certain condition or trait, across all studies for the population (such as a population with the same ethnicity/species, gender, age, habits, past medical history, suspected medical condition, surgical history, family history, prior genetic testing or analysis results, prior laboratory results, medications currently taking, medications previously taking, medications that may be given in the future, or any combination thereof), the aggregate number of organisms in the control cohort(s) across all studies (such as for a population with the same species, gender, age, , habits, , past medical history, suspected medical condition, surgical history, family history, prior genetic testing or analysis results, prior laboratory results, medications currently taking, medications previously taking, medications that may be given in the future, or any combination thereof), the aggregate number of total organisms in the studies (such as a population with the same species, gender, age, , habits, , past medical history, suspected medical condition, surgical history, , family history, prior genetic testing or analysis results, prior laboratory results, medications currently taking, medications previously taking, medications that may be given in the future, or any combination thereof), a rating of the journal(s) that publish the articles that the genetic variant-phenotype associations are from (such as an internal rating scale, the Impact Factor, the Immediacy Index, the Cited Half-life, or the Page Rank, such as discussed further below), the type of study (Genome Wide Association Study, Case-Controlled Study, Meta-Analysis Study, Prospective Study, Retrospective Study, etc.), the institution that conducted the study, the place the study was conducted (for example, United States, United Kingdom, Netherlands, Iceland, Norway, France, Italy, Japan, Australia, Spain, Russia, China, multicontinent, etc.), or the year the study was conducted.

[00188] The GVP Score is an example of a system used for rating a genetic variant-phenotype correlation (see for example, **FIG. 7**). It may be the only system used or combined with other systems, as further described below. Thus in the embodiments described herein, other rating systems

(such as those described below) may be used instead of the GVP score, or in combination with the GVP score. The GVP score may be population specific or it may not be population specific. In some embodiments, the GVP score is designated as 0 when there are 2 or more contradictory studies pertaining to the genetic variant and the phenotype, such as a disease or condition or, if there are three or more more studies pertaining to the same genetic variant-phenotype association in the same population then the score is a 0 when there is contradiction in one or more of the top three studies (including meta- analysis studies) with the highest power (the largest number of organisms in the study cohort); 0.25 for a single study with single disease cohort study population containing under 250 organisms; 0.50 for a single study with a single disease cohort study population containing over 250 organisms; 0.75 for a single study with two or more disease cohort study populations (each disease cohort population can be the same or different species or gender), with each containing under 250 organisms; 1 for a single study with two or more disease cohort study populations (each disease cohort population can be the same or different species or gender), each containing 250-999 organisms and each giving similar results; 1.25 for a single study with two or more disease cohort study populations (each disease cohort population can be the same or different species or gender), each containing over 1,000 organisms and each giving similar results; 1.50 for one primary study and one replication study, each with similar findings (same phenotype, such as disease, association and same direction of risk); 1.75 for one primary study with two or more replication studies, each with similar findings (same phenotype, such as disease, association and same direction of risk); 2 for two or more genome wide association studies (GWAS) with similar results; and 2 for a monogenic disorder where the genetic variant is found to segregate with the phenotype, such as a disease, or the genetic variant is found within a gene that has previously been associated with the phenotype, such as a disease, or likely to be associated with the phenotype, such as a disease, or laboratory (such as in vitro studies, in vivo studies, biochemical studies, molecular biology studies, computational models or studies, bioinformatic studies, phylogenetic studies, etc.) evidence that the genetic variant causes a change in the characteristics of its genetic sequence, a nearby genetic sequence, the protein produced from that gene, or a protein or molecule (such as microRNA) that interacts with the genetic sequence containing, or located near, the genetic variant. The designation of “contradictory studies” occurs when one study finds a statistically significant association between a genetic variant and a phenotype while another study finds a statistically non-significant association between that same genetic variant’s allele or genotype and the same phenotype or a genetic variant’s allele in tight linkage disequilibrium with the original genetic variant’s allele and the same phenotype. Contradictory studies may also exist when a study finds an opposite direction of association between the same allele or genotype of the same genetic variant and the same phenotype, such as if one study of a genetic variant finds increased risk of a phenotype while another study of the same genetic variant’s allele or genotype or a genetic variant’s allele in tight linkage disequilibrium with the original genetic variant’s allele finds decreased risk of the same phenotype. However, studies that find different degrees of

association (that are in the same direction) are not considered contradictory, such as, for example, if one study finds that a genetic variant's allele or genotype is associated with an increased risk of the phenotype with an odds ratio = 1.25 and a second study also finds an increased risk of the phenotype with an odds ratio = 1.65. This is considered confirmatory, not contradictory.

[00189] For example, if both study X and study Y are both case-controlled studies, both studied the same genetic variant or two genetic variants that are in linkage disequilibrium with each other, both looked at 1,500 and 5,000 African Americans in the study (disease) cohort, respectively, and both reported an increased risk of disease Z, then if the rating system as described above is utilized, the GVP score is 1.50 since there are two studies with similar results. The rating system being used, such as the GVP score, can be entered into the database along with the genetic variant (for example, the rs number from the dbSNP database, the chromosome that contains the genetic variant, the location of the genetic variant within a specific gene or chromosome such as its amino acid number and amino acid change (eg. Asp changed to Val at position 325) or the exact chromosome and chromosomal position as per Ensembl's coordinate numbering system, the specific sequence with 4, 5, 6, 8, 10, 15, 20, 30, 40, 50bp or more of sequence information surrounding and including the genetic variant included in the database or a linked database described herein, or some other type of identification that allows the exact position of the genetic variant to be discerned within the genome), and the risk information (such as the odds ratio or the relative risk or the hazard ratio or the absolute risk or the cumulative risk or some other value, either quantitative or qualitative), and the allele or genotype associated with the phenotype, as well as the specific population that this information is applicable to (such as species, gender, age, body mass index, , habits, past medical history, suspected medical condition, surgical history, family history, prior genetic testing or analysis results, prior laboratory results, medications currently taking, medications previously taking, medications that may be given in the future, or any combination thereof).

[00190] The rating system may also include Replication Status rating, such as whether an association between a genetic variant with a phenotype has been replicated in two or more studies (Yes), has not been replicated yet (No), has been replicated only in two or more disease cohorts within the same study (Within), or has failed replication in comparing two or more studies (Failed). The rating scales, including the Replication Status rating, are applicable to all types of genetic variant-phenotype associations, including multigenic, multifactorial, and monogenic. In some cases, such as for example for monogenic phenotypes, reported results can be considered very reliable even without replication of the results. Accordingly, in some embodiments of the present invention, a Replication Status of "Mono" can be assigned for monogenic phenotypes. In some cases, the replication status of "Mono" can be assigned for reported monogenic phenotypes that have not been replicated, indicating that they are nevertheless more reliable than non-replicated polygenic or multifactorial phenotypes, and a replication status of "Yes" or "Failed" can be assigned for monogenic phenotypes that have been replicated. In other cases, all monogenic phenotypes may be given a replication status of "Mono."

The Replication Status rating can be in addition to the GVP score or in-place of the GVP score. If there are three or more studies, where one or more contains data that is contradictory to the other studies (such as if two studies find a statistically significant association between a genetic variant's allele or genotype and a phenotype but a third does not) for the same population, then the studies with the highest power (number of organisms in the study cohort) are considered most relevant. If the top three studies (including meta-analysis studies) with the highest power (the number of organisms in the study cohort) confirm the same genetic variant's genotype-phenotype association (or if they confirm the phenotype association with two or more genetic variants' that are in linkage disequilibrium with each other), then the genetic variant's genotype-phenotype association is assigned a "Yes". If the top three studies with the highest power have contradictory results for the genetic variant's genotype-phenotype association, then the association is assigned a "Failed". As new studies are conducted and data released, this designation may change as a new study may have a high enough power to put it in the top three and therefore its results will be considered in the analysis and designation of "Yes", "No", or "Failed".

[00191] This rating system may be utilized to make the genetic analysis and final genetic report for an organism's genomic profile either more or less substantiated, or to include the genetic variant in some panels (further described below) or some genetic analysis (including, but not limited to, one or more of the following: analysis to calculate the risks such as predictive medicine risk, the calculation of organ risk, calculation of genetic health, and inclusion or exclusion of the genetic variant and its associated data within the genetic report) and not others. The genetic report may contain genotype information, genotype-phenotype associations, preventive medicine recommendations or interventions.

[00192] For example, an organism or their health care provider or manager or other third party, may request, order, obtain, or have an organism's genomic profile that provides only genetic variants associated with phenotypes that have a specific threshold value for one or more of the rating systems utilized. For example, the threshold value can be a specific value, such as above or below a specific value or it can be a range. For example, the threshold value for the GVP score can be above 1, below 1, or a range of values, such as any value between 0.25-1.25, any value not between 0.25-1.25. Alternatively, the threshold value can be a single numerical value such as 2. The analytical system is fully configurable so that any combination of threshold values for one or more rating systems can be combined in order to filter the analysis and results according to those selected thresholds. For example, **FIG. 6B** shows a genetic data analysis with a threshold GVP Score equal to or greater than 1.5, **FIG. 6C** which shows a genetic data analysis with a threshold of only monogenic phenotypes, and **FIG. 6D** which shows the threshold as being either Replicated associations or Monogenic phenotypes.

[00193] Highly substantiated associations, such that only those with a GVP score (rating) of 1.50 or above, or an even higher threshold of 1.75 or above, may be reported or determined, and all other genetic variants excluded. Alternatively, all possible associations and all genetic variants found

associated with a specific disease or a panel or an organ system can be included in the analysis, but those with contradictory studies are omitted, therefore the GVP score threshold is 0.25 or above. Thus, all genetic variants with a GVP score (also known as GVDC) of 0.25 or above that are associated with a specific phenotype, such as a disease, trait, condition or process, or that is included in a panel or an organ system, can or will be utilized in the analysis of predisposition and risk and may also be utilized to determine the Predictive Medicine Risk, organ score, genetic health score, or one or more of the above, and included within the genetic report.

[00194] The threshold value selected may be selected by the organism's whose genomic profile is being used, a health care manager of the organism, a medical professional, a medical entity such as a hospital, a laboratory director, or another third party. Alternatively, the threshold value may be determined by the party or entity, such as a company or laboratory generating the genetic data, as that party or entity may have one or more preset threshold values. Alternatively, the threshold values may be determined by an organism in consultation with the party or entity generating the genetic data, their health care manager or provider, or another third party.

[00195] The report for an organism's genomic profile may also contain all known associations, but the associations are divided into sections by the level of association. For example, the report may have section 1 that contains only genetic variant-phenotype (disease/trait/condition) score associations with a cut off of 1.75 or above, section 2 may contain genetic variant-phenotype (disease/trait/condition) score associations with a cut off of 1.5, section 3 may have a cut-off of 0.75-1.25, and section 4 may have a cut-off of 0.25-0.50. Furthermore, the reported GVP score may be changed at a later date. For example, an initial report for only highly substantiated associates can be generated for an organism, and a later report with all associations (i.e. a lower GVP score threshold value) is provided in a subsequent report. This rating system may also be updated, for example, by incorporation of new journal articles and data on an on-going basis. For instance, a genetic variant associated with a phenotype is assigned a GVP of 0.25 and another study is discovered or published that shows the same phenotype associated with the same genetic variant in the same population and the study and results are statistically significant. The GVP is then raised to 1.5. As a result, new reports can be generated based on incorporation of new journal articles and new studies and as a result new GVP score values for genetic-variant-phenotype associations. The new or updated reports may be produced from the initial data obtained from analyzing the genetic variants of an organism, the initial genetic sample obtained from an organism, or from a new sample. The new or updated reports may be provided for an additional fee.

[00196] In some embodiments, two or more different versions of the genetic report may be created utilizing this rating system. For example, a panel may be ordered for an organism through its cardiologist. The report produced for the cardiologist may only contain information on genetic variants and their phenotypes that have GVP score (coefficients) of 1.5 or greater while the report produced for the organism may contain information on genetic variants and their phenotypes with a

GVP score of 0.75 or greater. In other cases, the report produced for the cardiologist may only contain information on genetic variants and their phenotypes that have a GVP score of 0.75 or greater, while the report produced for the organism may contain information on genetic variants and their phenotypes with a GVP score of 0.75 or greater. As another example, a physician ordering the genetic testing and/or analysis may request a GVP score of 1.5 or greater but a medical researcher who is also working with the same subject may request a GVP score of 0.25 or greater. As another example, for a subject with an illness of unknown etiology, a physician may order the genetic testing and/or analysis with two different GVP scores, such that one report or one section of the report contains analysis and information pertaining to only GVP scores of 1.75 or greater while the second report or another section of the same report contains GVP scores of 0.5 or greater, thereby allowing the physician to assess not only the subject's risk or predisposition or affected status or carrier status for the phenotypes contained in the genetic testing and/or analysis panel ordered based on replicated research but to also receive information on genetic variants and phenotypes that are not replicated yet but may still provide useful information for the physician or the patient or both. Genetic analysis or genetic reports or both ordered with more than one GVP score threshold value may be provided for an additional fee.

[00197] Furthermore, in some embodiments, a specific genetic variant may have more than one GVP score, such as if it is associated with more than one phenotype. For example, the same genetic variant's genotype may be associated with increased risk for prostate cancer as well as a decreased risk for diabetes mellitus, type II. The GVP score for genotype-phenotype association with prostate cancer may be 1.5 while the GVP score for the genotype-phenotype association with diabetes mellitus, type II, may be 2. If the cut-off value for the GVP score is set at 1.75 and above, then this genetic variant and its data for diabetes mellitus, type II would be utilized in the analysis for diabetes mellitus, type II, in order to determine risk for diabetes mellitus, type II, including risk analysis, PMR, AS, organ score, or genetic health score, but this genetic variant would not be utilized in the analysis for prostate cancer as the GVP score threshold value is above the GVP score for the prostate cancer phenotype for that genetic variant.

[00198] In some aspects of the present invention, the aggregate number of organisms with the phenotype, such as a disease or condition, cohort(s) (also referred to as the disease cohort(s) or the study cohort(s)) such as described above for the GVP score, may be the sole factor or in combination with other systems described herein, for rating a genetic variant or genotypes and their correlations with one or more phenotypes. The rating system for the GVP score can include information pertaining to the number of studies (such as journal articles) that have shown an association between that exact genetic variant (or a genetic variant in linkage disequilibrium with that genetic variant, such as an $r^2 > 0.3$), as well as whether or not one or more of those studies is a Genome-Wide Association Study.

[00199] Other rating systems may be used instead of the GVP score, or in combination with the GVP score in evaluating the genetic variant-phenotype association. For example, all journal articles pertaining to genetic variants and their allele or genotype-phenotype association may be included automatically for computing a GVP score. Alternatively only specific journal articles, such as those decided to be added to the database or added to the genetic analysis or both, may be used. For example, the journal articles or publications may be analyzed before incorporating and storing both the article and its corresponding data and information within a database.

[00200] A journal article relating to one or more genetic variants and their association with any phenotype may be read and analyzed, by a human or automated to be fully accomplished or partially accomplished by a computer or other information technology system or software. A scaling system (such as numbers, letters, colors, symbols or combinations thereof) is then applied to the journal article based on numerous factors of that journal article. The factors of the journal article that are taken into account may contain the number of organisms in the disease (study) cohort, the number of organisms in the control cohort, the total number of organisms in the study, the institution that conducted the study, the place the study was conducted (such as state or country or region or continent), a rating for the journal itself (ratings may include, but not be limited to, an internal rating or the Impact-Factor of the journal, such as the system created by Eugene Garfield at this Institute for Scientific Information, the Immediacy Index of the journal (such as published in the Journal Citation Reports), the Cited Half-life of the journal, the Page Rank of the journal, or any other measure), the year the study was published, the type of study that was conducted (for example, Genome Wide Association Study (GWAS), Case-Control Study, Prospective Study, Retrospective Study, Meta-Analysis Study) the name of the journal, the name or reputation of any or all of the authors involved in the study, or any and all combinations of the factors thereof, such as shown in **Table 5**.

Table 5: Journal Article Factors

Journal Article Factors	Rating Scale
Number of organisms in Disease (Study) Cohort(s)	$<250 = 1$ $250-999 = 2$ $1000-2499 = 3$ $2500-4999 = 4$ $5000-9999 = 5$ $\geq 10,000 = 6$
Number of organisms in Control Cohort(s)	$<250 = 1$ $250-999 = 2$ $1000-2499 = 3$ $2500-4999 = 4$ $5000-9999 = 5$ $\geq 10,000 = 6$

Total Number of Organisms in the study	$<250 = 1$ $250-999 = 2$ $1000-2499 = 3$ $2500-4999 = 4$ $5000-9999 = 5$ $\geq 10,000 = 6$
Institution that Conducted Study	US News & World Report Ranking for Top Hospitals or Medical Institutions or Medical Schools $>\#50 = 1$ $11-50 = 2$ $\leq 10 = 3$ Outside of US & UK = 1 Wellcome Trust = 3 DeCode = 3 Broad Institute = 3 Multinational Study = 3
Place Study was Conducted	Eastern Europe = 1 Asia (Except Japan and Singapore) & Latin America & Middle East (Except Israel) = 2 Japan & Singapore & Israel = 3 Western Europe (Except UK) & Australia & New Zealand = 4 United States & United Kingdom = 5
Impact-Factor of Journal	$<10 = 1$ $11-25 = 2$ $26-35 = 3$ $>35 = 4$
Immediacy Index of Journal	$<3 = 1$ $3-4 = 2$ $>5 = 3$
Cited Half-Life of Journal	$<2 = 1$ $2-3 = 2$ $>3 = 3$
Page Rank of Journal	$<3 = 1$ $3-10 = 2$ $>10 = 3$
Year Study was Published	$<1980 = 1$ $1980-1989 = 2$ $1990-1994 = 3$ $1995-1999 = 4$ $2000-2003 = 5$ $2004-2006 = 6$ $>2006 = 7$
Type of Study	Retrospective or Prospective = 1 Case-controlled = 2 Meta-Analysis = 3 GWAS = 3
Name of Journal	Nature, Nature Genetics, Science, New England Journal of Medicine, Proceedings of the National Academy of Sciences, Cell, The Lancet, Journal of the American Medical Association = 3 All others = 1
Name/Reputation of Author(s)	Unknown = 1 One or more prior articles on same gene or gene family or disease = 2

[00201] The rating scale categories for a journal article, such as shown in **Table 5**, may be used organismly, or in various combinations, in determining a ranking system for the journal article, or in identifying a threshold value (such as described for GVP score herein), for including or excluding, the information in determining predisposition values, risk values, a genotype, a phenotype, or any such association between a genetic variant and a phenotype, such as a disease, trait, condition, or process. The rating or value given to a journal article may indicate that the journal article should be read or not read, that the journal article or its data should be included in the database or not included in the database, that the journal article or its data should be included in the genetic analysis of a person or not included in the genetic analysis, or that the journal article or its data should be included in the genetic report or not included in the genetic report.

[00202] For example, if the factors chosen to be analyzed include the number of organisms in disease cohort and impact factor of the journal, then the threshold may be: below 5 do not include in database, 5-6 include in database but not in genetic analysis, and 7 or greater to include in database and include in genetic analysis. For a journal article that contains 1,500 organisms in the disease cohort and is published in a journal with an impact factor of 36.98, the rating scale value would be $3 + 4 = 7$ and therefore the journal article, its data, or both are included in both the database and the genetic analysis. For a journal article that contains 5,000 organisms in the disease cohort and is published in a journal with an impact factor of 6, then the rating scale value would be $5 + 1 = 6$ and therefore the journal article, its data, or both is included in the database but not in the genetic analysis. For a journal article that contains 125 organisms in the disease cohort and its journal has an impact factor of 8, then the rating scale value would be $1 + 1 = 2$ and the journal article, its data, or both may not be analyzed and may not be included in the database or the genetic analysis.

[00203] Another rating system that may be used in combination with other systems described herein, or alone, is a rating system that determines whether or not the genetic variant's genotype-phenotype association for a specific genetic variant existing anywhere in the genome has been replicated, called the Replication Status. Replication can either mean two or more studies have shown the same direction (increased risk or decreased risk) for that genetic variant in the same or similar populations. An alternative system requires that at least 3 or more, 4 or more, 5 or more, etc. studies have arrived at similar results as stated above. Status of replication for each genetic variant can be designated either a simple Yes/No. Alternatively, status of replication can be a scale, such as Definitely Replicated, Moderately Replicated, Not Replicated Yet, or Failed Replication (if there are contradictory studies, such as a study that one or more studies that meet the threshold for the journal article factor(s) have shown no statistically significant genotype-phenotype association with that specific genetic variant or a genetic variant in linkage disequilibrium with that genetic variant). If a single study contains two or more separate disease cohorts and the genetic variant-phenotype association is similar in each cohort, then a separate rating of "Within" may be applied to the Replication Status for that genetic variant-phenotype association. Monogenic phenotypes can be also

be represented according to replication status, being assigned a replication status of “Mono” if the genetic variant is shown to segregate with the phenotype, if it occurs in a gene previously implicated with the phenotype, if it occurs in a gene suspected of being implicated with the phenotype, or if biochemical, molecular, phylogenetic, computational, or bioinformatic analysis shows that the genetic variant is most likely deleterious or harmful or likely to be associated with a disease or phenotype. If there are three or more studies, where one or more contains data that is contradictory to the other studies (such as if two studies find a statistically significant association between a genetic variant’s allele or genotype and a phenotype but a third does not) for the same population, then the studies with the highest power (number of organisms in the study cohort) are considered most relevant, as described herein.

[00204] This rating system may be utilized as described with the Replication Status, the GVP score or journal ranking system, in genetic analysis and generating genomic profiles and the genetic report by having more or less substantiated genetic variant-phenotype associations included or to include the genetic variant in some panels or genetic analysis (including one or more of the following: analysis to calculate the risk, the calculation of organ risk, calculation of genetic health, calculation of Predictive Medicine Risk, calculation of Notice Me Factor, calculation of action score, calculation of cumulative action score, and inclusion of the genetic variant and its data in the genetic report) and not others. For example, only replicated genetic variants may be included in the analysis of an organism’s genomic information. If so, only the genetic variants that are designated as replicated (i.e. a Replication Status of “Yes”) within the database, such as the Predictive Medicine Database, or a linked database may be included in the analysis and in the genetic report. Alternatively, the person who orders the genetic test and/or analysis may want to know all possible associations and to have all genetic variants found associated with a specific disease or a panel or a organ system regardless of replication status and therefore both genetic variants that are designated as replicated and those that are designated as not replicated may be included in the analysis. All genetic variants with a chosen Replication Rating (whether it be a Yes/No/Within/Failed/Mono designation or a scale as exemplified previously) can be utilized in the analysis of predisposition and risk and may also be utilized in determining the Predictive Medicine Risk, Notice Me Factor, Action Score, Cumulative Action Score, organ score or genetic health score.

[00205] Other systems for ranking, and that may be used for selection by an organism or their health care professional, manager or provider for analysis or inclusion in a genetic analysis, a genomic profile, or a genetic report include the Genetic Variant-Phenotype Triage (GVP Triage, see for example, **FIG. 8**), also known as the GVP-Clinical Significance Rating (GVP-CSR, or CSR). A GVP Triage can be ranked numerically, where 0 would indicate no clinical use, 1 would indicate limited clinical significance, value, or use, 2 would indicate moderate clinical significance, 3 would indicate very useful in a clinical setting, where a medical professional would likely find the result valuable, and 4 would indicate extreme clinical significance, such as a life-threatening condition. The GVP

Triage may be used also to determine whether genetic variants are included or excluded in genetic analysis or a report of the analysis. For example, genetic variants that have a GVP Triage of 2 or higher can be selected to be the only ones included in the analysis or report or both for an organism's genomic profile. Thus, similar to the aforementioned rating systems, GVP Triage values may serve as threshold values.

[00206] Each phenotype can have a separate GVP Triage rating assigned to it (for example, assigned by a licensed physician) for an increased risk of that phenotype and for a decreased risk of that phenotype. For monogenic phenotypes, each phenotype has a separate GVP Triage ratings assigned to it for the carrier state and for the affected state. The designation of carrier or affected is based on whether or not the genetic variant(s) associated with that phenotype are recessive or dominant in terms of Mendelian inheritance. For codominance, both alleles are considered dominant and the heterozygous genotype or diplotype may be associated with its own phenotype (such as Blood Type AB for the ABO blood group system in *Homo sapiens sapiens*) and for incomplete dominance, the heterozygous genotype may be associated with its own phenotype (such as with the Merle coat color trait in *Canis lupus familiaris* or with Sickle Cell Trait in *Homo sapiens sapiens*). As an example, for the hair color phenotype, the GVP Triage rating is "0" because hair color does not have clinical significance. However, for Long QT Syndrome, which can cause sudden death due to cardiac arrhythmias, the Long QT Syndrome phenotype is assigned a GVP Triage of "4" if the person is most likely affected with the syndrome because this information most likely requires immediate attention by a healthcare professional. Alternatively, if the person is a carrier of a genetic variant associated with Long QT Syndrome but is not affected by the syndrome, then this has less clinical significance and is assigned a rating of "2" because it is moderately useful (a healthcare professional may find this information useful in terms of educating their patient about the risk their children or future children may have in regards to Long QT Syndrome and also in educating their patient that a relative may carry or be affected by this syndrome and therefore may want to undergo genetic testing and/or analysis and health care professional consultation as well). The GVP Triage rating can occur at the genetic variant-phenotype level, so there is a GVP Triage rating (number) assigned to each genetic variant-phenotype association, meaning that there is at least one GVP Triage number assigned to each genetic variant.

[00207] The rating systems described herein may also be applied not to specific genetic variants but instead at the phenotype level, such as a disease, condition, or trait level. When this occurs, the rating system is no longer called GVP Triage but instead is called Clinical Significance Rating (CSR). The CSR is discussed below.

[00208] The Genetic Variant-Phenotype Rank (GVP Rank), also referred to as the SNP Ranking system, may be used to discern between genetic variants that are in linkage disequilibrium with each other (usually located within the same locus or within nearby loci) and that have been found to be, or can assumed to be, associated with the same signal or risk of the same phenotype. A GVP Rank may

be provided for any two or more genetic variants and their alleles that are in linkage disequilibrium with each other and that are associated with the same or similar phenotype and the same direction of risk (either increased risk or decreased risk or no risk). The genetic variant, such as an SNP, with the most significant statistical association with the phenotype is indicated by a special designation, such as the number 1, and is therefore the highest ranking genetic variant, such as an SNP. The genetic variant, such as an SNP, with the second most statistically significant association with the phenotype is then assigned 2. The genetic variant, such as an SNP, with the third most significant statistical association with the phenotype is then assigned 3, and so forth.

[00209] For example, genetic variant A, B, and C may all be associated with a predisposition for early-onset heart attack, with genetic variant A having an odds ratio = 1.40, genetic variant B having an odds ratio = 1.35, and genetic variant C having an odds ratio = 1.38. However, genetic variant A, B, and C are all in linkage disequilibrium with each other, with an $r^2=0.9$ between A-B, A-C, and B-C as indicated by The International HapMap Project (HapMap). Published research indicates that genetic variant A is the most statistically significant genetic variant associated with early-onset heart attack out of A, B, and C and is therefore assigned the GVP Rank of 1, genetic variant B is the second most significantly associated with that phenotype and is assigned GVP Rank of 2, while genetic variant C is the third most significantly associated and is assigned GVP Rank of 3. The Cardiovascular Genetic Testing Panel may be chosen by the organism and genetic testing and/or analysis may find that the organism's genotypes for genetic variant A, B, and C are all associated with increased risk for early-onset heart attack. However, it may be inappropriate to include the risk values, such as odds ratios, for genetic variant A, B, and C in the analysis to determine the risk of early-onset heart attack as the risks of genetic variant A, B, and C may not be mutually independent (they may all be associated with the same signal that predisposes to that phenotype). Therefore, during the analysis process, genetic variant A, which has the highest GVP Rank (1) is the only genetic variant that is utilized within the analysis while the other genetic variants (B and C) are not further analyzed. Only genetic variant A's risk value information and data is therefore utilized to ascertain the risk GCR and PMR for early-onset heart attack. Genetic variant A's risk and data can be entered into an algorithm or computation that takes into account other genetic variants (not in linkage disequilibrium with genetic variant A) or genetic variant A may be analyzed on its own. If the genotype associated with early-onset myocardial infarction for genetic variant A is not detected, but genetic variants B and C are both detected, then the next highest GVP Rank genetic variant is B, so B is utilized in the analysis and in any calculations to ascertain risk for early-onset heart attack while C is not utilized in the calculations.

[00210] This methodology can also be applicable to haplotypes and diplotypes. For example, it may be found that haplotype X, that contains genetic variants A, B, and C, is also associated with early-onset heart attacks with an odds ratio = 1.40 and is statistically more significant than A, B, or C alone. In this case, haplotype X is designated the GVP Rank of 1, genetic variant A is designated SNP

Ranking of 2, genetic variant B is designated SNP Ranking of 3, and genetic variant C is designated SNP Ranking of 4. If the genotype results for the genetic test and/or analysis contain the alleles at genetic variants A, B, and C that constitutes haplotype X then only haplotype X, along with its data and risk information, is utilized in the further analysis and calculation of the organism's risk for early-onset heart attack because haplotype X has the highest GVP Rank (1). If the alleles of either genetic variant A, B, or C however, do not satisfy haplotype X, then haplotype X does not exist and therefore the methodology looks at the next highest GVP Rank, 2, which is genetic variant A, and so forth until either an allele or genotype associated with early-onset heart attack is found and that genetic variant's risk value is the only one (out of those that are in linkage disequilibrium with it and have assigned GVP Rankings) utilized in the analysis and calculation of risk. This methodology can also be applied to any genetic variants within the same haplotype block as opposed to linkage disequilibrium, or both haplotype block data and linkage disequilibrium data can be utilized together. This methodology can also be applied to any genetic variants that have been shown in published literature to be associated with the same signal for a phenotype or for a risk or predisposition to a phenotype.

[00211] The rating systems and analytical methodology described herein, such as the journal ranking, GVP score, GVP Triage, Replication Status and GVP Rank can all be utilized independently of each other, or in any combination of two or more, and can be included as categories in a database described herein. For example, the GVP score, GVP triage, and GVP Rank can be utilized together such that only diseases with a GVP triage of 2 or above and only specific genetic variants and their specific allele or genotype-phenotype association with a GVP score of 1.5 or above, and only genetic variants that are mutually independent of each other (are either not in linkage disequilibrium or are in loose linkage disequilibrium, such as an $r^2=0.1$) may be included in the genetic testing, the genetic analysis and/or the Genetic Report.

[00212] The various rating systems may also be used to sort the results from genetic testing or analysis prior to any further analysis, processing, or the generation of the PMR, AS, CAS, or the genetic report. The various rating systems may also be used to choose and sort the genetic variants that will be tested for during the actual laboratory genetic testing and/or analysis process or the genetic variants that the laboratory will provide allele or genotypic information on. These rating systems offer significant control over what genetic variant-phenotype associations are included within the genetic testing, genetic analysis and genetic report and which are not, and allow for data to be pulled from a non-exclusionary Predictive Medicine Database that takes into account all known genetic variant-phenotype associations on the front end and allows for the filtering of these genetic variant-phenotype associations on the back end based on rating systems and thresholds as discussed.

[00213] Other rating systems may include the Phenotype's Clinical Significance Rating (CSR), which is a rating scale that assigns an integer (range is between 0 to 4) to each phenotype based on its clinical relevancy (for example, by a licensed physician or veterinarian), such as shown in **Table 6**.

The rating scale allows for phenotypes with greater clinical relevancy to be able to be discerned efficiently from those with less clinical relevancy. The CSR is one of the components of the Action Score; because of this, one of the ways the Action Score is weighted is by clinical significance.

Table 6: Clinical Significance Rating (Csr)

Description	Clinical Significance	Clinical Significance Rating (CSR)
No Clinical Significance –most likely not of importance to a healthcare professional. May be carrier of a monogenic phenotype with a CSR = 0-1 when affected.	None	0
Limited Clinical Significance – may be of limited importance to a healthcare professional. Prevention and/or treatment options for the phenotype may be severely limited, scarce, or highly experimental. Not yet able to limit morbidity or mortality even when predisposition is known prior to the manifestation of the phenotype. May also be phenotype with marginal clinical importance, such as Pityriasis capitis. May be carrier of a monogenic phenotype with a CSR = 2 when affected.	Limited	1
Moderate Clinical Significance – may be important to a healthcare professional as knowledge of a predisposition may aid diagnosis, although prevention and treatment options may be limited. May be able to limit morbidity with knowledge of predisposition. May also be phenotype that is fatal with mortality that may not be preventable or delayable but knowledge of predisposition may aid diagnosis. May be carrier of a monogenic phenotype with a CSR = 3-4 when affected	Moderate	2
High Clinical Significance – may be highly important to a healthcare professional, may be a clinically serious phenotype whose diagnosis may take significant time (months to years to decades) to make without prior knowledge of predisposition. While prevention and/or treatment options may exist, the phenotype may not be fully preventable but may be able to delay onset or significantly limit morbidity and/or mortality.	High	3
Critical Clinical Significance – may have critical importance to a healthcare professional, may aid the prevention and/or diagnosis of a very clinically serious phenotype, such as one that may cause sudden death. Phenotype or phenotype sequela usually preventable, manageable, or treatable. May be able to limit morbidity and/or mortality if predisposition or affected status is known for the phenotype. May be able to fully prevent or cure, either phenotype or phenotype sequela, if predisposition or affected status is known.	Critical	4

[00214] Each phenotype can have a separate CSR rating assigned to it (for example, by a licensed physician or veterinarian) for an increased risk of that phenotype and for a decreased risk of that phenotype. For monogenic phenotypes, each phenotype has a separate CSR rating assigned to it for the carrier state and for the affected or likely affected state (monogenic phenotypes with variable or

low penetrance or expressivity may be designated as 'likely-affected' instead of affected, because the manifestation of the phenotype and the degree of phenotype severity may have variability). The designation of carrier or affected is based on whether or not the genetic variant(s) associated with that phenotype are recessive or dominant in terms of Mendelian inheritance. Co-dominance and incomplete dominance may both be associated with unique phenotypes in the heterozygous state and those phenotypes will have their own CSR. A sample of phenotypes and their associated CSR ratings can be seen in **FIG. 6E-G**.

[00215] For example, for the hair color phenotype, the CSR rating is "0" because hair color does not have clinical significance. However, for Long QT Syndrome, which causes of sudden death due to cardiac arrhythmias, this phenotype is assigned a CAR rating of "4" if the person is most likely affected with the syndrome because this information may require immediate attention by a healthcare professional. Alternatively, if the person is a carrier of a genetic variant associated with Long QT Syndrome but is not affected by the syndrome, then this has less clinical significance and is assigned a rating of "2" because it is moderately useful (a healthcare professional may find this information useful in terms of educating their patient about the risk their children (or future generations) may have in regards to Long QT Syndrome and also in educating the patient that a family relative may carry or be affected by this syndrome and therefore they may want to discuss this with them and have the family talk with their physicians about this, as the family members may want to undergo genetic testing and/or analysis as well). Clinical significance and relevancy takes into account multiple factors (for example, by a licensed physician), such as whether or not a healthcare professional will find the information about a risk or predisposition or carrier status (including carrier, affected, or likely affected) for a specific phenotype useful. For example, the phenotype Amyotrophic Lateral Sclerosis (ALS) has very scarce preventive measures available and only limited treatment options. However, the phenotype may be difficult to diagnose at times, as it may take months or years before the proper diagnosis is made. Because of this, increased risk of ALS may be assigned a CSR = 2, as it may be of moderate importance to a healthcare provider as it may speed diagnosis and therefore limit the psychological turmoil that exists in patients with an illness of unknown etiology. A speedier and more efficient diagnosis may also limit the stress and psychological turmoil to the patient's family as well as the financial impact to the patient and the overall medical system, such as due to decreased physician visits or decreased number of tests or medications or both that are not specifically targeted at the true causative phenotype (the accurate diagnosis). Decreased risk of ALS may be assigned a CSR = 1, as ALS is already a rare phenotype so protection (decreased risk) against a rare phenotype has only limited clinical significance as it may help direct the healthcare professional away from ALS if their patient has a neurologic disease of unknown etiology and therefore knowledge of a decreased risk of ALS may be of marginal benefit to a healthcare professional. As another example, for the monogenic phenotype Arrhythmogenic Right Ventricular Cardiomyopathy (ARVC, also known as Arrhythmogenic Right Ventricular Dysplasia), a healthcare professional may most likely find

knowledge of a patient being affected by this phenotype (carrier status = affected or likely affected) as being of critical clinical significance because this phenotype may cause sudden death, it may cause sudden death as its presenting symptom, and also because there are numerous preventive measures that can be implemented to limit or avoid the sequela from the phenotype (such as sudden death). If an organism is known to have an ARVC associated genetic variant (and is found to be affected or likely affected), this information may be tremendously empowering to a healthcare professional and may possibly lead to life-saving interventions and preventive measures. The CSR is similar to the GVP Triage but occurs at the phenotype level, while GVP Triage occurs at the genetic variant-phenotype level. This allows for the sorting and filtering of data at multiple levels, as well as threshold values to be implemented throughout the analytical process at multiple levels and augments operator control through providing multiple data filtering levels.

[00216] Other rating systems may include the Phenotype Impact Rating (PIR), such as shown in Table 7. The PIR is a rating scale that assigns an integer (such as an integer ranging from -3 to +3) to each phenotype based on the impact that phenotype may have upon the person. The PIR allows phenotypes beneficial to survival to be discerned efficiently from phenotypes that are detrimental to survival, and also phenotypes that are more beneficial or those that are more detrimental to be discerned efficiently from those that are less beneficial or detrimental. A separate PIR is assigned to monogenic carrier, monogenic affected, multifactorial decreased risk, and multifactorial increased risk. Polygenic phenotypes are assumed to follow a multifactorial model throughout the analytical process.

[00217] Each phenotype can have a separate PIR rating assigned to it (for example, by a licensed physician or veterinarian) for an increased risk of that phenotype and for a decreased risk of that phenotype. For monogenic phenotypes, each phenotype can have a separate PIR rating assigned to it for the carrier state and for the affected state. The designation of carrier or affected is typically based on whether or not the genetic variant(s) associated with that phenotype are recessive or dominant in terms of Mendelian inheritance. As an example, the phenotype of 'Increased Longevity' is assigned a "+3" if there is an increased risk of that phenotype. For a disease such as Crohn's Disease, if there is an increased risk of that disease then the PIR is "-2" because it is a very serious chronic disease but is usually not life-threatening. If there is a decreased risk of Crohn's disease, however, the assigned PIR is "+1" because it is slightly beneficial to be protected against this disease but since most organisms don't have Crohn's disease and since protection against Crohn's disease won't significantly augment or prolong life (or decrease the morbidity or mortality of any other diseases), decreased risk of this disease has less of an impact upon a person than an increased risk of the disease (which is why increased risk for Crohn's disease is assigned a "-2" while decreased risk is assigned a "+1"). The PIR is one of the components of the Action Score; because of this, one of the ways the Action Score is weighted is by how beneficial or how harmful that specific phenotype is.

Table 7: Phenotype Impact Rating (PIR)

Phenotypic Effect	Phenotype Impact Rating (PIR)
Causes sudden death or severely debilitating disease	-3
Serious disease or difficult to treat/cure condition	-2
Manageable disease	-1
Neutral phenotype	0
Slightly helpful trait or ability	+1
Moderately helpful trait or ability	+2
Significantly Advantageous trait or ability	+3

[00218] The aforementioned rating systems can be used in ranking genetic variants and phenotypes. For example, based on the ratings or rankings, genetic variants associated with phenotypes can be selected for analysis to generate a genetic profile and/or a genetic report tailored to a specific organism.

[00219] Analysis may include determining the Cumulative Genetic Risk (CGR) and the Predictive Medicine Lifetime Risk (PMR) for polygenic or multifactorial phenotypes by analyzing all (one or more) relevant (based on information known and rating systems applied, such as GVP Score and GVP Triage) genetic variants that are associated with that phenotype. The Cumulative Genetic Risk (CGR), also known as the Genetic Cumulative Risk (GCR), is the organism's cumulative genetic risk for polygenic or multifactorial phenotypes based on comprehensive analysis of their relevant genetic variants that are associated with the specific phenotype. Relevant genetic variant(s) can be selected based on those that make the cut-off threshold for analysis, as previously described. In many cases, genetic variants have three possible genotypes: Allele1/Allele1, Allele1/Allele2, or Allele2/Allele2. In some embodiments, the first step in calculating the CGR is to convert the odds ratios associated with the alleles or genotypes of all the relevant genetic variants associated with that specific phenotype into relative risks. In some embodiments, odds ratios are converted into relative risks as described by Zhang and Yu (*JAMA* 280:1690-1691 (1998)). The genotype frequency, from sources available in the arts, such as The International HapMap Project (www.hapmap.org) for each of the three possible genotypes for each of the genetic variants is then multiplied by the relative risks for each of the three genotypes for each relevant genetic variant associated with that phenotype. The HapMap population used to ascertain these values is matched as closely as possible with the population of the organism who is currently undergoing genetic analysis (for example, if the organism is an European American, then the 'CEU' HapMap frequencies are utilized in the calculation). The resulting three values (genotype frequencies multiplied by relative risks for all three possible genotypes) for the genetic variant are then added together and produce a single number for each genetic variant. This value is then multiplied together for all relevant genetic variants detected during genetic testing and the resulting value is referred to as the Generic Population Risk Load (GPL). Next, the organism's genotype is considered at each of the relevant genetic variants and the relative risks associated with each of those relevant genetic variants (based on that genetic variant's genotype for that organism) are multiplied together to create a single value, known as the Proband Risk Load (PRL). The cumulative

relative risk for an organism, also known as their Genetic Cumulative Risk (GCR) or their Cumulative Genetic Risk (CGR) is: $CGR = PLR / GPL$. An exemplary embodiment describing a method for determining a cumulative genetic risk for an organism is provided herein as **Example 5**.

[00220] The Predictive Medicine Lifetime Risk (PMR) is the new lifetime risk for an organism for polygenic or multifactorial phenotypes based on their gender-matched population specific Generic Lifetime Risk (GLR) and their own CGR. The $PMR = (GLR) \times (CGR)$. Monogenic phenotypes are typically reported as a 'carrier status', which is analyzed and reported as non-carrier and non-affected, carrier but not affected, or affected. The degree to which the organism may be affected may also be reported, such as the potential age of onset, severity, penetrance or expressivity. An exemplary embodiment describing a method for determining a Predictive Medicine Lifetime Risk for an organism is provided herein as **Example 5**.

[00221] Utilizing this methodology, the genetic report may contain a comprehensive analysis of both risk, predisposition and carrier status for the organism. Some phenotypes are associated with both monogenic and multifactorial inheritance. In some cases, monogenic genetic variants may be analyzed as monogenic variants that may be deterministic of a phenotype, while multifactorial variants that predispose to the phenotype may be analyzed separately, as described herein for multifactorial phenotypes, and the results of the monogenic analysis and the multifactorial analysis may either be reported together or separately in the genetic report.

[00222] In some cases, a genetic report may contain information concerning an organism's risk of, predisposition for, or carrier status for two or more multifactorial phenotypes and two or more monogenic phenotypes. In some cases, a genetic report may contain information concerning an organism's risk of, predisposition for, or carrier status for: two or more multifactorial phenotypes; and one or more monogenic phenotypes, two or more monogenic phenotypes, three or more monogenic phenotypes, five or more monogenic phenotypes, ten or more monogenic phenotypes, twenty or more monogenic phenotypes, or fifty or more monogenic phenotypes. In some cases, a genetic report may contain information concerning an organism's risk of, predisposition for, or carrier status for: two or more monogenic phenotypes; and one or more multifactorial phenotypes, two or more multifactorial phenotypes, three or more multifactorial phenotypes, five or more multifactorial phenotypes, ten or more multifactorial phenotypes, twenty or more multifactorial phenotypes, or fifty or more multifactorial phenotypes. Sometimes, the number of multifactorial or monogenic phenotypes reported is "no more than" a certain number, e.g., no more than ten, no more than fifteen, no more than twenty, no more than thirty, no more than fifty, no more than one hundred, no more than two hundred, or no more than five hundred phenotypes.

[00223] Select genetic variants of clinical significance may be independently reported on or discussed in the genetic report. The genetic variants reported or discussed may be associated with monogenic or polygenic phenotypes or risk for multifactorial phenotypes. Some genetic variants may be included in the report, even if the predictive medicine risk or action score for that multifactorial phenotype is not

included in the genetic report, such as if it does not make a certain threshold or cut-off value. For example, a single nucleotide polymorphism in the ITGB3 gene on (ITGB3 Chr. 17: 42715729 Y) is associated with premature coronary events and other phenotypes associated with premature heart disease and treatment effectiveness for heart disease. If the genotype for this SNP is found to convey increased risk of these phenotypes, the risk value for that genotype is applied to an algorithm, along with all other relevant genetic variants for that specific phenotype, but regardless of the AS or PMR for that phenotype, the genetic report may still specifically mention this genetic variant and its phenotype associations, as this SNP has been shown to be responsible for considerable morbidity and mortality and has clinical utility on its own. The determination of what multifactorial risk genetic variants are of special clinical utility and significance or the designation of genetic variants as having special clinical significance may be made by a licensed medical physician or veterinarian and can be automatically reported on (included) in the genetic report. Alternatively, genetic variants-phenotype associations with a specific GVP Triage level or phenotypes with a specific CSR may be chosen for inclusion within the genetic report regardless of the phenotypes ultimate AS or PMR.

[00224] Specific genetic variant(s) that are tested for whose allele(s) or genotype(s) deduced are found to not be associated with risk for a phenotype may also be included within the genetic report, so that the organism who for which the genetic report was ordered, or their physician or veterinarian or other third party, is aware that the specific genetic variant or phenotype or both is tested for but the phenotype associated allele(s) or genotype(s) isn't detected or no increased or decreased risk is ascertained based on the allele(s) or genotype(s) that are detected through the genetic testing and analysis. For example, if the organism is found to not have the major cystic fibrosis related deletion, referred to as the delta-F508 mutation (CFTR Chr. 7: 116986883-116986885 delTTT), then the genetic report may specifically indicate that this clinically significant genetic variant is not detected. A list of some or all genes or genetic variants or both tested for, regardless of whether or not their alleles or genotypes are associated with increased or decreased risk or no change in risk of a multifactorial phenotype or a carrier or affected of a polygenic or monogenic phenotype, as well as a list of some or all of the phenotypes that are tested for, may or may not be included in the genetic report and may or may not appear in a separate section of the genetic report. The genetic variants with the greatest significance, such as those that are more frequently the cause of, or are associated with, the phenotype, (such as those with higher overall phenotype-associated allele or phenotype-associated genotype frequencies or those associated with a higher population attributable risk) may be listed first or in a separate section compared to those genetic variants that appear less frequently (such as those with lower overall phenotype-associated allele or phenotype-associated genotype frequencies or those associated with a lower population attributable risk) as the cause of, or associated with, the phenotype in a single population, throughout multiple populations, or throughout all populations.

[00225] The Generic Lifetime Risk (GLR), as previously stated, is the gender-specific population lifetime risk for a specific phenotype prior to any genetic analysis, which may be represented as a

percentage or be able to be converted to a percentage. This data can be obtained from published literature and from sources available in the arts including, but not limited to, published journal articles, national governmental health and disease services agencies or departments (such as the Health and Human Services in the United States or the National Health Service in the United Kingdom), including all of the agencies and divisions of the primary governmental health agency such as the United States Department of Health and Human Services (HHS) and all of its agencies and divisions including the United States' Centers of Disease Control and Prevention (CDC) and the United States' National Institutes of Health (NIH) as well as all its divisions, such as the National Cancer Institute (NCI). For example, the Generic Lifetime Risk at birth for Diabetes Mellitus, Type II for European Americans is 0.312 for females and 0.267 for males, for African Americans it is 0.490 for females and 0.402 for males, and for Hispanic Americans it is 0.525 for females and 0.454 for males (*Narayan et al. JAMA 290(14):1884-1890 (2003)*) As another example, the Generic Lifetime Risk for Melanoma at birth for European American's is 0.0173 for females and 0.0256 for males, for African American's is 0.0009 for females and 0.0007 for males, for Hispanic American's is 0.0058 for females and 0.0052 for males, for Asian American's is 0.0016 for females and 0.0017 for males, and for Native American's is 0.0024 for females and 0.0034 for males. (National Cancer Institute's Surveillance, Epidemiology and End Results (SEER), seer.cancer.gov/csr/1975_2005/results_merged/topic_lifetime_risk.pdf).

[00226] The Generic Lifetime Risk can be dependent on the age of an organism. For example, the GLR for Lung Cancer for Hispanic Americans is 0.0363 for females and 0.0526 for males at birth and 0.0369 for females and 0.0548 for males at age 40, for African Americans the GLR for Lung Cancer is 0.0545 for females and 0.0775 for males at birth and 0.0569 for females and 0.0847 for males at age 40, for Asian Americans the GLR for Lung Cancer is 0.0428 for females and 0.0703 for males at birth and 0.0432 and 0.0719 for males at age 40, for Native Americans the GLR for Lung Cancer is 0.0487 for females and 0.0527 for males at birth and 0.0510 for females and 0.0575 for males at age 40, and the GLR for Lung Cancer for European Americans is 0.0652 for females and 0.0786 for males at birth and 0.0665 for females and 0.0819 for males at age 40. (National Cancer Institute's Surveillance, Epidemiology and End Results (SEER), seer.cancer.gov/csr/1975_2005/results_merged/topic_lifetime_risk.pdf) Generic Lifetime Risk can be determined for gender-specific populations for each phenotype both from birth and at different ages. In some cases, phenotypes are described as a "susceptibility to", or an "increased risk of", this susceptibility or risk may refer to genetic variants that provide for an increased risk as compared to the species and/or gender and/or age matched population generic lifetime risk values. Protection against may refer to a decreased risk or no risk as compared to the ethnicity and/or gender and/or age matched population generic risk values.

[00227] Prevalence rates, incidence rates, and heritability for phenotypes can be obtained through sources available in the arts, such as, but not limited to published literature and various public

resources, such as previously described, including the HHS and its CDC or the NCI. If exact gender-specific population statistics (incidence rates or prevalence rates or both for a phenotype) do not exist, then comparable statistics may be utilized, such as determined by a geneticist, an epidemiologist or a licensed physician or veterinarian. For example, incidence rates of phenotype A may not be known for African American males but it is known for African Americans in-general (females + males), this value would be used until a value specific for African American males is reported or obtained. In other embodiments, prevalence rates of phenotype B is not currently known for European American females but it is known for Western European Caucasian females, and this value is used until a value specific for European American females is reported or obtained.

[00228] The GLR and PMR can be used to calculate the Percent Change in Lifetime Risk. The Percent Change in Lifetime Risk calculates the percent change between the GLR for a phenotype (for example, ascertained from journal articles or published records, such as from the CDC or NCI, as previously described) and the calculated PMR. The formula for the percent change in lifetime risk is: Percent change in Lifetime Risk = $((\text{PMR}-\text{GLR})/\text{GLR}) \times 100$.

[00229] The Notice Me Factor (NMF) allows for the conversion of a range of percent change in lifetime risk into a single integer congruent to the scale of integers utilized with the CSR and the PIR. This NMF is one component of the Action Score; because of this, one of the ways the Action Score is weighted is by the NMF which is, in turn, determined by the Percent Change in Lifetime Risk. This is used because while some phenotypes may have high clinical significance (and therefore have a high CSR) and also be very detrimental to a person's health (and therefore have a negative PIR), the genetic variants, when analyzed together, may not increase or decrease the lifetime risk of that disease significantly.

[00230] For example, for increased risk of diabetes mellitus, type II, the CSR = 3 because diabetes mellitus, type II is a significant health issue whose negative effects can be either avoided or minimized through either preventive measures or early-detection and treatment and the PIR = -2 because it is a serious chronic disease. However, if the Predictive Medicine Lifetime Risk of diabetes mellitus, type II, is 49.1% for an Hispanic American male organism, this represents only an 8.14% increase over the Generic Lifetime risk of 45.4% for an Hispanic American male. This Percent Change in Lifetime Risk most likely is not of significance to a practicing healthcare provider and therefore it is assigned a low NMF(NMF = 1). However, if the Predictive Medicine Lifetime Risk of diabetes mellitus, type II, is instead 64.3%, then this represents a 41.6% increase over the Generic Lifetime Risk and is much more likely to be significant to a practicing healthcare provider and therefore it is assigned a much higher NMF (NMF = 10).

Table 8: Notice Me Factor (NMF)

Percent Change	Notice Me Factor (NMF)
< -50	20
-50 to -20	10

-19.99 to -10	5
-9.99 to -0.01	1
0	0
0.01 to 9.99	1
10 to 19.99	5
20 to 50	10
> 50	20

[00231] The Action Score (AS) is a combination of the Clinical Significance Rating (CSR), the Phenotype Impact Rating (PIR), and the Notice Me Factor (NMF). These three numbers allow for the action score to be weighted by clinical significance, phenotype benefit or harm, and also the degree to which a person's genetic profile affects their risk for that phenotype. The formula used to calculate the action score is: Action Score = CSR x PIR x NMF

[00232] The Action Score can allow both the healthcare provider and the organism to efficiently discern which phenotypes they need to focus on in terms of understanding, education, surveillance, treatment and/or preventive measures. The more negative the Action Score, the more significant the harmful risk is for a specific phenotype based on the person's genetic profile. The more positive the Action Score, the more significant the beneficial value is for a specific phenotype based on the person's genetic profile.

[00233] A color-coding system may be used in an organism's genetic profile. For example, a shade of a red color may be used to depict a significantly harmful phenotype, whereas a shade of a blue color may be used to depict a significantly beneficial phenotype. **Table 9** illustrates some embodiments, however, other colors may be correlated with different AS ranges, and other AS ranges may be used.

Table 9A: Action Score Color Scheme

Action Score (AS)	Action	Action Score Color
> 60	Very High	Navy Blue
41 to 60	High	Airforce Blue
21 to 40	Medium	Baby Blue
11 to 20	Low	Alice Blue
-10 to 10	Nothing	Tea Green
-11 to -20	Low	Seashell
-21 to -40	Medium	Lavender Rose
-41 to -60	High	Hollywood Cerise
< -60	Very High	Crimson

Table 9B: Action Score Color Scheme

Action Score (AS)	Action	Action Score Color
> 60	Very High	Navy Blue
41 to 60	High	Airforce Blue
21 to 40	Medium	Baby Blue
11 to 20	Low	Alice Blue
0 to 10	Nothing	Cream
-10 to 0	Nothing	Cream

-11 to -20	Low	Seashell
-21 to -40	Medium	Lavender Rose
-41 to -60	High	Hollywood Cerise
< -60	Very High	Crimson

[00234] The risks for phenotypes, can also be used to determine scores for one or more specific organ systems, or specialties, such as, but not limited to those shown in **FIG. 10** and listed in **Table 10**.

Table 10: Organ Systems/ Specialties

Organ Systems / Medical Specialties
Anesthesiology & Critical Care
Cardiology
Dental
Dermatology
Temperament
Learning & Intelligence
Trainability
Milk Production
Meat Production
Ear, Nose & Throat
Endocrinology - Pancreas
Endocrinology - Thyroid
Endocrinology - Misc
Fertility
Gastroenterology & Hepatology
Geriatric's Health
Gynecology
Hematology
Immunology & Allergy
Infectious Disease
Laryngology
Men's Health
Metabolic & Rare Diseases
Musculoskeletal
Nephrology
Neurology
Newborn's Health
Nutrition, Exercise & Weight
Obstetrics & Fetology
Oncology - Reproductive Organs
Oncology - Lung
Oncology - GI
Oncology - Misc
Ophthalmology
Otology
Pediatrics & Neonatology
Pharmacology & Toxicology
Psychiatry
Pulmonology
Reproductive Health
Rheumatology
Sexuality

Surgery
Syndromes
Traits & Special Abilities
Urology
Vascular
Women's Health

[00235] For example, a cardiovascular score, which indicates the genetic health for an organism's cardiovascular system, can be determined by integrating the risk factors for each of the specific conditions and diseases affecting the cardiovascular system of an organism. Scores for organ systems or medical specialties can include the risk factors determined from the genetic profile and can further include information obtained from the organism. Organ systems or medical specialties can include cardiovascular; heart; lung; laryngology and dental; laryngology; dental; nutrition, exercise, and weight; otology; pediatrics and/or neonatology; pulmonology; anesthesiology and critical care; dermatology; development and learning; ear, nose, and throat; endocrinology; gastroenterology and hepatology; gastroenterology; hepatology; gall bladder; liver; thyroid; pancreas; gynecology; hematology; oncology; hematology and oncology; immunology; immunology and allergy; infectious diseases; metabolic diseases; metabolic diseases and rare diseases; rare diseases; men's health, musculoskeletal; neonatology; neurology; obstetrics; obstetrics and fetology; ophthalmology; pharmacology, toxicology and anesthesiology; pharmacology; toxicology; anesthesiology; psychiatry; psychiatry and addictions; rheumatology; sexuality; sexuality; sexuality and fertility; sleep medicine; surgery; syndromes; traits and special abilities; urology and nephrology; urology; nephrology; vascular; geriatric health; gender-specific health and women's health, as well as any others that appear in **Table 10** or are discussed herein.

[00236] A series of panels are described herein that aggregate genetic variants into comprehensive panels that provide information about an organism's risks and in some cases, options, in a targeted area. A list of panels is provided in **Table 14**. **FIGS. 15-20** disclose specific panels. The panels of genetic variants provide a profile of the health and risks that detail not only one or more diseases or conditions but also the genetic variants associated with the efficacy of drugs that may be utilized to treat the diseases or conditions or the genetic variants linked to habits that are linked to the disease. For example, there are genetic variants involving habits, such as eating particular foods, which increase or decrease one's risk of a disease based on another genetic variant. Thus, identifying these genetic variants and the related phenotype may allow one to alter his or her life and impact the ultimate result of one's genes. The panels are chosen to combine those genetic variants that will provide composite information about the genetic profile along with additional variants beneficial to the subject's assessment and/or use of the information. These panels are newly created and offer beneficial advantages that allow one to identify the optimal medical intervention, medication, dosage of a drug, or adverse impacts of a drug at an earlier stage and thus avoid serious delays in crucial treatment. The panels serve a variety of functions for analyzing a group of genetic variants of an

organism and in some embodiments allow one to evaluate the suitability of an organism for therapeutics, suitability for medical interventions such as surgery, transplantations (donor or recipient), psychiatric treatment, or treatment associated with other medical specialties described herein; or identify the best candidates for career recruitment or training such as for military or police work. The panels, in some cases, aggregate diverse genetic variants to provide a valuable profile of organisms that allows significant benefits in their overall treatment or management of life choices to improve health and, in some instances, longevity.

[00237] The panels of genetic variants may be performed on an organism simultaneously or over periods of time depending on the outcome of some of the tests completed. For example, some panels may include variants considered to be reflex phenotypes that may be follow-on evaluations depending upon the outcome of a first phenotype. These reflex phenotypes provide useful additional screening of the genome to determine the presence of valuable variants that will contribute to earlier intervention and reduce wasted treatments or eliminate dead ends in therapy. Reflex testing and reflex phenotypes are further discussed herein.

[00238] The different organ systems or medical specialties can be represented by different panels. The panels comprise groups of phenotypes, including conditions, traits, diseases, and disorders, and corresponding genes and loci that can be tested. In some cases, the panels may comprise arrays, probes, primers or sequences that may be used to determine an organism's carrier status or risk of, or predisposition for, a phenotype, such as a condition, disease, disorder or trait.

[00239] The panel may also be a Custom Panel where an organism's owner or third party can choose any phenotype from any of the panels described herein. An organism's owner or third party can choose different sets of any phenotypes from any of the panels or from a complete list of all phenotypes available, such as a Custom 10 Panel, which tests for 10 phenotypes or a Custom 20 Panel, which tests for 20 phenotypes. Custom panels can range from two phenotypes to over 1,000 phenotypes. Furthermore, an organism may choose any panel or set of panels for various other options (**FIG. 21**). For example, any panel or specific phenotype may be used for the Offspring Projection through the Combined Analyses of Different Organisms (OP-CADI) Option (which is further described herein). For the Only Decreased Risk Option, any panel or specific phenotype may be designated as "Protection Only" at the request of an organism or healthcare provider. This designation means that only phenotypes that show a lower risk value (protection against the phenotype) are utilized for the organ system color or are included in the Genetic Report or both. Those phenotypes that the organism is found to be at increased risk for may then not appear in the Genetic Report. For the Only Increased Risk Option, any panel or phenotype may be designated as "Increased Risk Only" at the request of an organism. This designation means that only phenotypes that show a higher risk value (higher risk for the phenotype) are utilized for the organ system color or are included in the Genetic Report or both. Those phenotypes that the organism is found to be at decreased risk for may then not appear in the Genetic Report. For the Specific Disease Exclusion

Option, any phenotype(s) may be chosen to be excluded from being included in the analysis, and in the calculation of the organ system score and color, the genetic health score and color, and in the Genetic Report. If the raw genotypic data is saved and identifiable, then the organism may choose to have this Exclusion Option revoked at a later time so that all phenotypes that were excluded are analyzed (which may incur an additional fee). If the organism's raw genotypic data is not identifiable, then new genetic material may have to be obtained and the genetic testing rerun at the laboratory (which may incur an additional fee).

[00240] The panels also describe various genes and loci that may be used to detect the risk of the various phenotypes, such as diseases or traits, but it should be clear that other genetic variations in other genes and loci that are correlated with the various phenotypes, such as diseases or traits, can also be used. In some embodiments, variants that are thought to be significant in determining a phenotype, may include, but not be limited to, those described in **FIGS. 22A-22P**. Furthermore, the phenotypes, such as diseases or traits, listed may also be a general disease category, such as cancer, which may include a variety of types.

[00241] Each phenotype, such as a condition, that is found to have either an increased risk or decreased risk may be factored into a genetic algorithm under one or more organ system / medical specialty categories. This links the results from the panel to a genetic analysis algorithm, which then computes the genetic health score for each organ system / medical specialty tested for within that panel and then an overall genetic health score. This information is then utilized to produce one or more genetic reports, which contains information including, but not limited to, preventive recommendations and/or interventions based upon the results of the comprehensive genetic testing results and analysis.

[00242] An organ system score, or medical specialty score, can be determined from at least 2 specific phenotypes, such as conditions, diseases or traits, of an organ system or medical specialty. Other organ system scores may be determined from at least 3, 4, 5, 6, 7, 8, 9, or 10 specific phenotypes, including conditions, diseases, disorders, or traits. An organism or third party, such as for example a medical professional, may choose to have carrier status or risks or both for a subset of phenotypes (also referred to herein as conditions, diseases or traits) listed in a panel to be determined. Alternatively, an organism or third party may choose to have one or more of carrier status or risks or predispositions for a subset of phenotypes, such as conditions, listed in a panel to not be determined or reported to them. For example, an organism may choose at least 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 20, 25, or all of the conditions of a panel to be analyzed or determined for their genetic profile. Alternatively, an organism may choose at least 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 20, or 25 of the conditions of a panel to not be analyzed or determined for their genetic profile.

[00243] An organ system score may be determined from a subset of the phenotypes, such as conditions, chosen or from all of the phenotypes, such as conditions. If a subset is chosen, the organism or third party may further choose to have carrier status or risks or both for other phenotypes,

such as conditions, listed in a panel be determined after the initial risk or carrier status or both determination of a subset of phenotypes, such as conditions, listed on a panel, and the subsequent results can be added to the initial organ system score. Each phenotype, such as a trait, condition or disease, tested may be assigned to one or more of categories of organ systems or medical specialties (such as by a licensed physician or veterinarian) and such assignment can be factored into a genetic health score for each organ system/medical specialty. An overall genetic health score, described further below, can be determined using an algorithm that takes into account all of this information. An organism can be notified directly, or through a third party, on a recurring basis, such as for example every 3 to 6 months, or 6 months to yearly, or when the phenotype may become relevant (such as when the organism turns a specific age or when a specific milestone or event is met, such as for example if through genetic testing and analysis an organism is found to be at increased or decreased risk for West Nile Virus susceptibility and an increase in regional West Nile Virus infection cases occurs or an epidemic or pandemic occurs), about any updates, such as to changes in their predictive medicine score or their genetic health scores.

[00244] In some cases, the disclosure provides for monitoring of local, state, national, and/or international trends (e.g., rates of infection, increases in infection, decreases in infection, or outbreaks) of diseases, disorders or conditions or any infectious or transmittable disease or condition. Significant changes in local, state, national, and/or international trends may be associated with organisms who fit certain geographic criteria e.g., they reside or travel, or plan to reside or travel, in the local, state, or international area identified with the changing trend). Identified organisms who are found to be at increased or decreased risk for the infectious or transmittable disease, disorder or condition may then be notified of this change. The notification service may be offered for an additional fee, such as for example a subscription fee. The notification may include an updated genetic report, or updated predictive medicine score(s) or genetic health score(s).

[00245] In some embodiments, the predisposition, risk and/or carrier status of an organism may be determined for a subset of phenotypes, e.g., a subset of phenotypes listed in the Cattle Lifecycle & Economic Productivity Panel (**FIGS. 15I-15J**) or any other panel provided herein. A cardiovascular system score may be determined from this subset. The organism may further choose to have his or her predisposition, risk, and/or carrier status for other phenotypes, listed in a panel to be determined after the initial risk and/or carrier status determination of the first subset of phenotypes (e.g., diseases, disorders, traits or conditions) is determined. The second set of results can be integrated into the initial cardiovascular system score to obtain a new score.

[00246] A “subset” may refer to any number of phenotypes (e.g., diseases, disorders, traits or conditions) less than the entire list of phenotypes, (e.g., diseases, disorders, traits or conditions) for a panel. In some cases, the subset of phenotypes (e.g., diseases, disorders, traits or conditions) can be tested separately from the subsequent set of phenotypes. A single sample may be tested for an initial subset of phenotypes, (e.g., diseases, disorders, traits or conditions) and a subsequent sample may be

tested for subsequent phenotypes (e.g., diseases, disorders, traits or conditions). Alternatively, a single sample can be used to determine the carrier status, predisposition or risk of an organism for of all the phenotypes of a single panel, but only a subset of the results are reported to the organism initially.

[00247] A single sample may also be used to generate results from more than 1 panel. For example, a single sample may be used to generate results from 2 or more, 3 or more, 4 or more, 5 or more, or all of the panels.

[00248] Results from a subset of the panels may be reported. For example, all the phenotypes, such as conditions, of a subset of the panels (subset refers to any number of panels less than all the panels, including a single panel out of 2 or more panels) can be reported. Alternatively, a subset of the phenotypes (e.g., diseases, disorders, conditions or traits) of a subset of panels can be reported. Results from all the panels can also be reported to the organism. For example, all the phenotypes from all the panels, or a subset of phenotypes from all the panels can be used to generate a report. Phenotypes (e.g., diseases, disorders, traits or conditions) not reported initially can be subsequently reported, for example, after an organism consults with his or her physician, genetic counselor, physician assistant, nurse practitioner, other healthcare professional or other third party. Some examples of reporting a phenotype after an event subsequent to the initial genetic analysis, e.g., after the organism consults with a physician, are provided when the concept of “reflex testing” is described herein.

[00249] A single panel or combinations of the different panels may be used to generate a single organ system score. The genetic profiles can have one or more organ system scores. For example, at least 2, 3, 4, 5, 6, 7, 8, 9, or 10 organ system scores may be determined from a genetic profile. The organ system score can be selected by an organism or their health care provider or other third party. Selection can be based on an organism’s consultation with one or more of the following: his or her genetic counselor, a managing doctor, a nurse practitioner, a physician assistant, a healthcare provider, a parent or legal guardian such as if the organism is a minor, a health care proxy, an advisor, or another third party. The score can be indicated numerically or by color, as described above. The score, or color, can be a Cumulative Action Score (CAS) or an Indicator of Genetic Health of Organ System. For example, in one embodiment, the color red would be used for scores less than -10 for an organism’s genetic profile, indicating highly important to discuss with organism and may be highly important for organism to follow-up with their physician or specialist based on this information. Pink can be used for scores between -1 to -10 to indicate moderately important risk. Green can be used for scores of 0 to indicate no pertinent deleterious or protective information discovered although organ system was accessed. Blue can be used for scores between +1 to +10, to indicate moderately important protection. Gold can be used for scores >+10 indicating very beneficial protection, and no color can be used for an Organ System or Medical Specialty that is not accessed, for example, if an

organism chose a genetic testing panel or package that did not contain information about this system or specialty.

[00250] In one embodiment, the CAS is calculated by adding all the organism Action Scores for all the phenotypes that fall under the same Medical Specialty or Organ System. To calculate CAS, the following formula may be used for N number of Action Scores, with the minimum value that N can be is equal to 1, is: $CAS = (AS_1 + AS_2 + \dots + AS_N)/N$. If there is only one action score ($N=1$), then the formula is $CAS = AS_1/1 = AS_1$.

[00251] Each Action Score can be calculated such that each AS has a CSR, a PIR, and a NMF integrated into it, and as a result, the score is weighted in terms of clinical significance, degree of phenotype benefit or harm, and significance of the change in risk. Therefore, each organism Action Score may be added together and divided by the total number of Action Scores available that are applicable for that specific medical specialty or organ system. A single action score can be applicable to one or more medical specialties or organ systems.

[00252] The CAS is also known as the System Score because it gives a score to each organ system and medical specialties that apply to the body. The System Score can be used in determining the organ system of greatest and least concern in terms of significant harmful risk for an organism and in terms of significant decreased risk for an organism. A System Score may be calculated for each organ system (that can also be defined in terms of a medical specialty) and a System Color can be assigned to that organ system. Other coloring schemes can also be used, as well as other system score ranges may also be used. The coloring system can efficiently convey the organ systems and medical specialties of greater concern and those that are of lesser concern. The System Score and the System Color can also be altered or changed with a change in non-genetic factors, such as decreasing red meat consumption and this change or potential change may conveyed in the genetic report. Even information surrounding non-genetic factors, such as red meat consumption, can be genetically tailored to the individual as specific genetic variants are known to increase the risk of colorectal cancer with red meat consumption to a greater degree in people with a specific variant – therefore, people with this variant can be specifically advised of their increased risk and that decreasing red meat consumption may decrease their risk of the disease.

[00253] The coloring can appear throughout a report for an organism's genetic profile, such as on tabs for each organ system and medical specialty, on a face or cover of the genetic report or one of the initial pages that displays a picture of the entire human body, with each organ system shaded by its System color and its score may also be indicated, or the coloring may appear in other locations throughout the report. The System Color can represent an indicator of the health of each medical specialty or organ system based on the person's genetic profile. For organ systems and medical specialties that are not accessed in that panel, no coloring appears for the System Color.

Table 11: Color Scheme for System Score

System Score	System Color	Relevancy
> 60	Navy Blue	Highly Beneficial or Protective
41 to 60	Airforce Blue	Beneficial or Protective
21 to 40	Baby Blue	Moderately Beneficial or Protective
11 to 20	Alice Blue	Slightly Beneficial or Protective
-10 to 10	Tea Green	No pertinent risk or protective information is discovered although medical specialty or organ system was accessed.
-11 to -20	Seashell	Slightly Deleterious or Harmful
-21 to -40	Lavender Rose	Moderately Deleterious or Harmful
-41 to -60	Hollywood Cerise	Deleterious or Harmful
< -60	Crimson	Highly Deleterious or Harmful
No Score Available	No Color	Medical specialty or organ system was not accessed

[00254] The panels that can provide genetic phenotype, such as condition, predisposition risks or carrier status or both for each organ system/healthcare specialty organismly and can be grouped together to generate a total, overall, or cumulative genetic health score, based on all genetic organ/specialty scores combined (described further below). As described herein, thousands of genetic variants and polymorphisms, including but not limited to, single nucleotide polymorphisms (SNPs), mutations, insertion/deletion polymorphisms (in/dels or DIPs), copy number variations (CNVs), repeats, translocations, inversions, gene expression levels and methylation status, can be detected at a single time. Variants that increase risk and those that decrease risk can be evaluated, as well as variants that are associated with either being a carrier of a phenotype or having or likely having a phenotype can be evaluated, providing a more complete view of a person's overall genetic health. The thousands of genetic variants, such as polymorphisms, and their associated phenotypes can be interconnected in a matrix, as previously discussed (see for example, **FIG. 13D, E**) and the matrix can be assessed and analyzed for each organism based on reflex testing (see for example, **FIG. 13A-C**) (reflex testing is further described, herein).

[00255] The organ system scores, CAS, or results from the panels, can also be used to generate a genetic health score. The overall genetic health score can be generated from one or more phenotypes such as the phenotypes in a panel, a subset of the phenotypes in a panel, the phenotypes in a group of panels, a subset of phenotypes in a group of panels, or for a number of organ systems, medical specialties. All the Cumulative Action Scores that are calculated can be added together to obtain a Genetic Health Score, for all organ systems and medical specialties, which is an overall genetic health score, an indicator of genetic wellness. The indicator can be a word, such as high, medium, or low, or ranging from extremely good, good, neutral, poor, extremely poor. The genetic health score can be a number, for example, ranging from 0 to 5, wherein 0 indicates an extremely poor genetic wellness, which indicates a high risk to serious disease or condition and a 5 indicates an extremely high genetic wellness, indicating extremely low risk of medical conditions. The genetic health score can also be a percentage, such as a high percentage indicating a high likelihood or risk of disease and a low

percentage indicating a low likelihood or risk of disease. Genetic health score or genetic wellness can also be expressed in a range of colors, for example, red indicating a high risk of having poor general health or predisposition to poor general health, yellow for average, and blue for an extremely high genetic wellness, with low risk of having diseases or conditions.

[00256] In some embodiments, the Genetic Health Score is a single score that takes into account all System Scores that already have had all action scores factored into them. This provides for a single score that can be used to compare an organism's Genetic Health Score to others, as well as to see how an organism's Genetic Health Score changes over time with non-genetic factors, such as if an obese person institutes weight loss measures such as modifications, such as dieting and exercise, or by taking medications, such as sibutramine, or by having surgery, such as gastric bypass surgery or gastric banding, and is able to significantly decrease their body mass index. As with the CAS, each Genetic Health Score range can have a specific color associated with it (Table 12). Other colors and score ranges may also be used. The formula used to calculate the Genetic Health Score for a N number of Cumulative Action Scores, with the minimum value that N can be is equal to 1, is: Genetic Health Score = $(CAS_1 + CAS_2 + \dots + CAS_N)/N$.

Table 12: Color Scheme for Genetic Health Score

Genetic Health Score	Color
> 60	Navy Blue
41 to 60	Airforce Blue
21 to 40	Baby Blue
11 to 20	Alice Blue
-10 to 10	Tea Green
-11 to -20	Seashell
-21 to -40	Lavender Rose
-41 to -60	Hollywood Cerise
< -60	Crimson
No Score Available	No Color

[00257] In some embodiments, the genetic analysis of the present invention may provide an aggregate score of the PMRs associated with a group of related phenotypes. In another example, a set of phenotypes may be identified as related to gender specific health. The aggregate score may be calculated in the same manner as a cumulative action score as described herein. In some cases, the aggregate score may be referred to as a gender specific health score.

[00258] In another example, a set of phenotypes may be identified as related to reproduction.. The aggregate score may be calculated in the same manner as a cumulative action score as described herein. In some cases, the aggregate score may be referred to as a pediatrics score, a reproduction score, or a reproduction/pediatrics score.

[00259] In another example, a set of phenotypes may be identified as related to the research. Such phenotypes may include but are not limited to one or more of the phenotypes, two or more of the phenotypes, or five or more phenotypes listed in Research-related panels. The aggregate score may be calculated in the same manner as a cumulative action score as described herein. In some cases, the

aggregate score may be referred to as a military score, military recruitment score, or military suitability score.

[00260] In some embodiments, an organism's owner may view how the organism's Predictive Medicine Risk for each phenotype, his or her action scores, his or her cumulative actions scores, his or her longevity score, his or her gender specific health score, his or her pediatrics or reproduction score, his or her suitability-for-companions or service or sports or production, his or her medical care score, his or her reproductive health score, or gender-specific health score, changes based on certain variables, such as if he or she follows preventive recommendations or interventions or the advice of his or her physician or other third party.

[00261] The change in risk values may be static, such as being printed in the genetic report, or dynamic, such as when the organism is meeting with a genetic counselor or nurse practitioner or physician assistant or other third party or if they are reviewing their results on the internet, such as on a webpage. Thus, organisms may be able to see how risk values would change (which may be represented by changes in the number values of the PMR, the AS, the CAS, or the genetic health score, changes in their colors, or verbally conveyed by a healthcare professional or one or more of the above) by checking off boxes associated with specific preventive measures or verbally agreeing to follow or choosing certain preventive measures. The organism's owner may be able to visualize these changes on a display, such as a computer screen, holographic image, monitor, or television. This may apply to any change in a non-genetic (environmental) factor (such as habits including eating habits and sexual habits, addictions, medications taken or not taken, compliance with medical advice, etc.)

[00262] In some embodiments, an organism's owner may view how their Predictive Medicine Risk for each phenotype, their action scores, their cumulative actions scores, and their genetic health score changes based on certain variables, such as if they change their habits or if they do not follow the treatment regimen. For example, if a subject takes regular exams, such as an annual check-up, by a physician, such as a veterinarian, or both (the increase in risk may be separate values for each potential change in habits or preventive recommendation or intervention that they choose not to follow and the increase in risk may also be a different separate value when two or more preventive recommendations or interventions are combined). This change in risk values may be static, such as being printed in the genetic report, or dynamic, such as when the organism is meeting with a genetic counselor or nurse practitioner or physician assistant or other third party or if they are reviewing their results on the internet, such as on a webpage. Thus, organisms may be able to see how risk values would change (which may be represented by changes in the number values of the PMR, the AS, the CAS, or the genetic health score, changes in their colors, or verbally conveyed by a healthcare professional or one or more of the above) by checking off boxes associated with specific preventive measures or verbally agreeing to follow or choosing certain preventive measures. The organism may be able to visualize these changes on a display, such as a computer screen, holographic image, monitor, or television. This may apply to any change in a non-genetic (environmental) factor (such as

habits including eating habits and sexual habits, addictions, medications taken or not taken, compliance with medical advice, etc.)

[00263] Prior to obtaining a genetic profile an organism may be “pre-tested”, for example as shown in **FIG. 1**. An organism’s owner or representative or third party (**102**) can directly contact a central location (**104**), or a health care practitioner’s office or other facility providing genetic testing and/or analysis, regarding genetic testing and/or analysis and obtain pre-testing consultation. Pre-testing may include a confidential meeting between the organism and a physician, genetic counselor, nurse practitioner, physician assistant, nurse, other healthcare provider or other third party. During the “pre-test”, an organism’s owner or representative or third party can consult with the healthcare provider, such as a genetic counselor, veterinarian or other third party who may suggest what type of genetic profile may be suitable for the organism based on the organism’s owner or guardian’s concerns or information from a questionnaire the organism’s owner or guardian fills out.

[00264] Thus, when calculating an organism’s risk or predisposition for a phenotype, specific condition or set of conditions, the computer system and genetic analysis algorithm may take into account factors concerning the organism, including but not limited to: gender, age, weight, non-genetic (environmental) factors and habits, medications, alternative therapies, present medical symptoms, the organism’s family history for a disease, disorder or condition (including confirmed, presumed, or suspected diagnoses), the organism’s own medical history (including confirmed, presumed, or suspected diagnoses), results from a physical examination, results from a medical test, answers from a questionnaire filled out by the owner of the organism, or other phenotypes, such as a condition, disease, disorder, or trait, of an organism or other factor described herein.

[00265] The questionnaire may be specific to an organism owner’s concerns.

[00266] An organism’s pedigree can be generated from the questionnaire (for example, as in **FIG. 2**). The genetic pedigree can be analyzed by a physician, genetic counselor, physician assistant, nurse practitioner, or other healthcare provider and used in combination with other information from the questionnaire in determining what genetic testing, analysis or level of services should be performed. Based on the pre-testing (such as the results from the questionnaire or after consultation with a healthcare professional or both), an organism can decide what type of genetic profile or services he or she wants. The services can be customized to serve various cross sections of the society. For example, the phenotype, such as disease or condition, panels can be comprehensive, including many phenotypes, such as conditions, or limited, including one or two phenotypes, such as conditions. The number of phenotypes, such as diseases or conditions, offered can be determined by socio-economic need of an organism agreeing to receive comprehensive genetic analysis and a genetic profile. Other levels of service with varying costs to the organism can include genetic profiles with more than one phenotype, such as a disease or trait, amount of pre-test or post-test (follow-up) interaction with a health care provider or both, type of panel chosen, number of panels chosen, if OP-CADI is chosen, if reflex testing is chosen as well as the degree and depth of reflex testing chosen, or phenotypes chosen.

[00267] Another level of service can be a comprehensive genetic profile or choice of panels. Other levels of service may depend on the type of panel chosen. Other panels may be specific for testing the presence of various genetic variants for phenotypes, such as conditions, diseases or traits, of particular interest for a group of organisms. The organisms interested in the panels may choose to have their genetic profile determined from a single panel, a number of panels, or a subset of phenotypes, such as conditions and traits, from a panel. Alternatively, the organism's owner or representative or third party may also choose phenotypes, such as diseases or traits, to make a Custom Panel. For example, an organism may choose a Custom 10 Panel, which tests for 10 phenotypes, such as diseases, conditions or traits, the organism chooses, or a Custom 20 Panel, which tests for 20 phenotypes, such as diseases, conditions or traits. The Custom Panel may have approximately 3, 5, 10, 15, 20, 25, 30, or more phenotypes, such as diseases, conditions or traits. Thus, an organism can choose different demoninations, such as a Custom 10 Panel, which tests for 10 phenotypes or a Custom 20 Panel, which tests for 20 phenotypes. Custom panels can range from one phenotype to over 1,000 phenotypes. An organism may make the choice after consultation with one or more of the following: GC, physician, nurse practitioner, physician assistant, or other healthcare provider or other third party. Reflex testing refers to the process wherein the determination of the risk, predisposition, or carrier status of an organism for one or more phenotypes, leads to, triggeres, or causes another phenotype to be genotyped or not to be genotyped, to be analyzed or to not be analyzed, to be included in a report or not to be included in a report, to be included in a specific section of the report or not to be included in a specific section of the report, or any combination thereof.

[00268] The initial phenotype, such as a condition, disease, disorder, trait or addiction, may receive a positive or a negative result, and the reflex phenotype may be, but is not limited to, one or more of the following: a different phenotype, a phenotype related to the initial phenotype (e.g., indicator(s) of severity of initial phenotype, age of onset of initial phenotype, degree of penetrance or expressivity of initial phenotype (for example if the initial phenotype is coronary artery disease, the reflex testing may report on genetic variants that are indicators of the degree of severity of coronary atherosclerosis in coronary artery disease), a response to a type of treatment for the initial phenotype (e.g., adverse reaction to a medication used to treat or prevent the initial phenotype, ability to metabolize a medication used to treat the initial phenotype, indicators of what medications will or will not be most effective in treating or preventing the initial phenotype, dosing of medications to treat or prevent initial phenotype, outcome of surgery to treat the initial phenotype, or adverse reactions from surgery to treat the initial phenotype).

[00269] The predicted phenotype Outcome of Surgery includes whether or not the surgical procedure is likely to be successful in treating a disease or a symptom of a disease, either in the short-term or long-term of both. The initial phenotype may be a specific disease and the reflex phenotype may be a response to, or a sensitivity to, or effectiveness of, or adverse reaction to, a specific drug used to treat or prevent the disease. For example, an organism may be found to be at risk of breast cancer, and the

reflex phenotype tested is the organism's response to, or sensitivity to, the drug tamoxifen. The results of the reflex testing of an organism's response to, or sensitivity to, tamoxifen may be reported simultaneously with the risk of breast cancer or may not be reported simultaneously but instead reported at a later time, such as if or when the organism is diagnosed with breast cancer.

[00270] In other cases, an organism may be found to be at risk of an initial phenotype that is an addiction and the reflex phenotype, such as a condition, to be tested is a disease or disorder that can result from the addiction. For example, an organism may be found to be at risk for nicotine addiction, which reflexes to the condition of risk of developing lung cancer .

[00271] The reflex testing can be for risk of, predisposition to, or carrier status for more than one phenotype.

[00272] The results from such testing may help guide decisions as to, for example, what preventive measures, such as genetically tailored prevention, the organism's owners or representative or third party should follow, what medication the organism should take, whether the organism should follow a particular diet and/or exercise program, whether the organism should be fed a specific diet, whether a particular surgery should be performed or alternative surgeries or treatments considered, what kind of medical screenings the organism should have, and the like.

[00273] Other examples of reflex testing are disclosure herein, however, the present invention is not limited to those listed. The indications for reflex testing may not rely on genotypes of genetic variants but instead may be due to a quality or action or diagnosis of the organism that the genetic sample is from.

[00274] Another example is if the organism, medical professional, entity or third-party ordering the genetic profile indicates that they do not want to be tested for or notified of the results for a certain disease, but genetic variants that increase the person's risk of that disease are found, then the reflex takes into account the request not to be notified (known as the 'specific disease exclusion option') and these results do not appear in the report or in the analysis of the neurologic organ system or the overall genetic health score or appear elsewhere and the results may or may not be stored in person's raw genotypic data or the person's raw analytic data that is either saved by the company conducting the genetic testing and analysis or by the person or entity or third-party or by the organism that the genetic sample is from or who ordered the test. The specific disease exclusion option may also be dependent upon the results of reflex testing. This applies to all phenotypes and all options available, such as specific disease exclusion option, only decreased-risk option, only increased-risk option, and OP-CADI.

[00275] Reflex testing may also be a level of service that is provided. By testing for many different phenotypes, such as conditions, disorder, traits and diseases, including monogenic, polygenic, and multifactorial phenotypes, and by utilizing a robust and powerful database combined with genetic, heuristic, or other algorithms, reflex testing can be conducted in which a test result leads to operator-engagement or automatic engagement by an analysis system, such as a computer system, to examine

other genetic variants of significance given those first results. Thus, if a significant result is found for a specific phenotype, such as a disease, disorder, trait or condition listed in **FIGS. 15-20**, Reflex Testing can automatically or manually report the associated phenotypes (e.g., diseases, disorders, traits or conditions) such as those shown in **FIGS. 15- 20**. A schematic of reflex testing is depicted in **FIGs. 13A-C**. In some embodiments, there may be only a first and second round. In some cases, a positive or negative result for a first or an initial phenotype (e.g., disease, disorder, trait or condition) may reflex to the testing for a second phenotype (e.g., disease, disorder, trait or condition) and a positive, or negative, result for the second phenotype may reflex again to testing a third phenotype (e.g., disease, disorder, trait or condition) such as depicted in **FIGs. 13A-C**.

[00276] In some examples, the initial test result, phenotype, or genetic analysis may show either increased or decreased risk for a phenotype, such as a condition, or a carrier of a phenotype, or affected or likely affected by a phenotype. Other initial results may include having, being suspected of having, or being diagnosed with a phenotype, or having a family member that has or is suspected of having or is diagnosed with a phenotype. In other cases, or if an organism may be prescribed, or be taking, a certain medication or supplement. In other cases, an event that may trigger a reflex test may be that an organism reaches a certain milestone, such as a specific age or age range, or that an organism starts to go through puberty such as gonadarche, thelarche, or menarche, or weaning, or initiation of reproduction.

[00277] In some cases, a positive result for a phenotype may reflex to testing for or analyzing a second or reflex phenotypes that is related to, or associated with, the first phenotype. In some cases, there may be a chain of three or more reflexes, so that an initial phenotype reflexes to a second phenotype or multiple second phenotypes; a second phenotype, (or multiple second phenotypes) reflexes to a third phenotype, (or multiple third phenotypes,); and a third phenotype reflexes to a fourth phenotype (or multiple fourth phenotype, such as depicted in **FIG. 13**) and so on. An initial phenotype may lead to testing, analyzing, and/or reporting a chain of 1 or more, 2 or more, 3 or more, 4 or more, 5 or more, 10 or more, 15 or more, or 20 or more reflex phenotypes. For example, an initial phenotype may lead to testing, analyzing or reporting of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 30, 50, 100, 200, or 500 reflex phenotypes. In other cases, a negative result may be obtained for the initial phenotype (e.g., disease, disorder, trait or condition). The negative result may or may not be confirmed by repeating the test. The confirmation may or may not warrant any further reflex test.

[00278] Additional rounds of reflex testing may incur additional costs to an organism, or to his or her health care provider, or to a third party, such as an insurance provider. For instance, a low-cost service may be available whereas no reflex testing is available for any of the panel or phenotypes or both, a medium-cost service may be available where reflex testing goes only to round 2 and no further, and a high-cost service may be available where reflex testing goes through as many rounds as needed until no further reflex testing rounds exist. As another example, any additional reflex rounds

beyond the initial first round may incur an additional fee, either all together or separately (each subsequent reflex round may represent another additional fee).

[00279] Reflex testing may be time independent or time dependent. The updated reflex analysis and reporting may also take into account any new data, such as new genetic variant-phenotype association data, and updated information in regards to the initial round of testing, such as for coronary artery disease in the example above, so that both the updated initial round of testing and the reflex round of testing (which may also be updated with the most recent information) will be reported at time B, after the initial genetic testing and analysis is conducted at earlier time A. The genetic testing analysis and reporting of results may be based on the initial DNA sample received from the organism, or a new DNA sample received at some later time, and may be based on the raw or already analyzed genetic testing data obtained from the initial genetic testing or from raw or already analyzed genetic testing data obtained from the organism since that initial time.

[00280] The organism's owner(s), representative(2), a healthcare provider or other third party may be able to request a partial or full reflex analysis at any time or if certain events occurs or milestones are reached, so that , for example, at an early age such as for example 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 12, 14, 15, 17 ,18, 20, 21, 30 years or older, full reflex analysis can be analyzed and reported to the organism for phenotypes that may not affect that organism until they are older. The genetic testing, analysis and reporting of results may be based on the initial DNA sample received from the organism, or a new DNA sample received at some later time, and may be based on the raw or already analyzed genetic testing data obtained from the initial genetic testing or from raw or already analyzed genetic testing data obtained from the organism since that initial time.

[00281] Reflex testing may automatically report relevant information to the organism, the organism's parents or legal guardians, the organism's health care proxy, the organism's physician or other healthcare provider, or a third-party, based on the age of the organism or other factors, such as if that organism is ever suspected of having or is diagnosed with a phenotype, such as a disease. This reporting may occur by a written update to the genetic report, an email, a text message, an auditory alert, a manual or an automatic addition to the organism's medical record, a facsimile transmission, a verbal communication over the telephone, internet, or in person, or through an internet conference or website. The organism or any third party receiving this reporting may be able to turn on or off automatic reporting as per their own preference. The genetic testing analysis and reporting of results may be based on the initial DNA sample received from the organism, or a new DNA sample received at some later time, and may be based on the raw or already analyzed genetic testing data obtained from the initial genetic testing or from raw or already analyzed genetic testing data obtained from the organism since that initial time. This manual or automatic reporting of reflex testing analysis may incur an additional fee.

[00282] In some examples, a patient or organism may choose to have only one level of reflex testing and/or analysis with his or her genetic analysis but, after reading the genetic report and, optionally,

consulting with his or her healthcare provider, the patient or organism may decide to have further reflex testing and/or analysis or full reflex testing and/or analysis conducted that may then detect the carrier status, predisposition, or risk of said organism for one or more previously unreported phenotypes.

[00283] Even if a phenotype is not initially reported at time A, genetic testing and analysis, or genotyping on its own without any analysis (which gives raw genotypic data for one or more genetic variants or genes or chromosomes or the full exome or the full genome), may be conducted at time A, and the genetic analysis or genetic reporting or both containing information about both the initial round of analysis and carrier status and risk for those initial phenotypes as well as any information pertaining to reflex rounds, may not be reported to the organism, the organism's parents or legal guardians, the organism's health care proxy, the organism's physician or other healthcare provider, or a third party, until a later date or a specific milestone, which can be, such as for example, the organism's age or age range, or when an organism starts to go through puberty such as gonadarche, thelarche, or menarche, or if the owner, or representative, or third party of the organism is thinking of engaging the organism in or are participating in an amateur or professional sport, or is planning to or trying to get pregnant, or when the organism starts or ends menopause or andropause, or if the organism dies, or if the organism's owner or representative or third party is thinking of moving or moves the organism to a different region such as a new state or country or continent or move from a rural to urban or from an urban to rural environment, or if there is a public health epidemiologic event, such as the changes in the incidence, prevalence or surveillance of a disease.

[00284] The genetic testing analysis and reporting of results may be based on the initial DNA sample received from the organism, or a new DNA sample received at some later time, and may be based on the raw or already analyzed genetic testing data obtained from the initial genetic testing or from raw or already analyzed genetic testing data obtained from the organism since that initial time. Reflex testing may also be contingent upon actual diagnosis at earlier time A as the initial factor and then either genetic testing (the actual genotyping) or genetic analysis (of genotypic data) is conducted, or both, at later time B (which constitutes reflex testing because it is based off of the initial factor of a diagnosis) to ascertain one or more other phenotypes. The analysis of genetic information and the reporting of phenotypes or panels or both or the reporting of genetic variants or genotypes or both or the analysis of genetic variants and their associated phenotype(s) is not dependent upon time.

[00285] In some embodiments, a newborn may have his or her full genome sequenced and may have the raw data analyzed near or at that time when he or she is born, time A, or analyzed at a later time, time B, and reported at time B or reported at a later time, time C.

[00286] When these panels are ordered at a later time, either the phenotypes and analysis may already have been conducted at an earlier time and therefore the results are just reported on and displayed at this later time, or the raw data is both analyzed and then reported on at this later time B or C. The analysis and reporting of panels and phenotypic information, both risk and carrier information, is

therefore not time dependent upon when the actual genetic testing (e.g., the actual genotyping to ascertain the raw genotypic data) is conducted. The panel(s) to be analyzed and reported on can be chosen or paid for or both at the initial time of genetic testing (e.g., the actual genotyping when the raw genotypic data is obtained) or at a later time or both. If the raw genotypic data is ascertained at an earlier time and a panel is chosen and analyzed and reported on at a later time, either the original data concerning risk values of specific genetic variant-phenotype associations and carrier status may be used or updated data concerning risk values of specific genetic variant-phenotype associations and carrier status may be used. The original algorithm that is being utilized when the raw genotypic data is ascertained (e.g., from when the genetic testing was conducted) may be used or a new algorithm may be used. The genetic sample may also be obtained at a different time or at the same time as when the genetic testing (to ascertain the raw genotypic data) is conducted. This manual or automatic reporting of initial analysis of results or reflex testing analysis either at the time of the actual genetic testing or at a later time or both may incur an additional fee.

[00287] Genetic testing that ascertains an organism's genotype at one or more places in the genetic code may be conducted at time A and the genetic analysis or the genetic reporting or both may be conducted at a later time, time B. For example, full genome sequencing may ascertain an embryo's or newborn's genetic code and this genetic code may be analyzed or reported on or both, in part or in full, immediately or not until a later time, such as seconds, minutes, hours, days, weeks, months, years, or even decades in the future after the initial testing and/or analysis occurred. If specific groups of phenotypes or genes are tested for and/or analyzed and/or reported on, then that specific group of phenotypes or genes may constitute a specific panel, regardless of where or when the testing (genotyping, sequencing, or any other genetic testing methodology described herein), analysis, or reporting occurs.

[00288] The milestones that trigger the reporting of either the results of the initial round of genetic analysis and reporting or one or more reflex rounds of analysis and reporting or both at some time (either instantaneous or seconds to minutes to days to weeks to years to decades) after the initial genetic sample has been obtained (and either stored or genetic variants tested for or sequencing or full sequencing conducted so that raw genotypic data is obtained, such as genotypes at one or more positions within the genome) and preliminary analysis conducted (and either a report generated or no report generated or an abbreviated report generated with only some information) may be determined either by the service provider of the genetic analysis and genetic reporting or may be determined by the organism, the organism's parents or legal guardians, health care proxy, physician, genetic counselor, physician assistant, nurse practitioner, veterinarian, owner, representative, healthcare provider, or third party.

[00289] The genetic testing analysis and reporting of results may be based on the initial DNA sample received from the organism, or a new DNA sample received at some later time, and may be based on the raw or already analyzed genetic testing data obtained from the initial genetic testing or from raw

or already analyzed genetic testing data obtained from the organism since that initial time. This reporting can be either automatic, such as being notified automatically by e-mail, written report, in-person, telephone, facsimile, text message, webpage, or web conference or manual, such as if the organism must do something in order to access the analysis and results, such as accessing a specific website or calling a number, visiting an office, or contacting a third party in order to receive the analysis and results. Milestones that trigger reporting of initial analysis results or reflex testing analysis results, or both, is applicable to all species, including humans and non-humans, such as livestock and pets.

[00290] Reflex testing may be performed for organisms that are human as well as non-humans. Organisms may be human as well as other mammals (Mammalia) or Aves or Fish or Reptilia or other eukaryotes (such as Fungus or Protists) or prokaryotes (such as Bacteria and Archaea) or virus (including retroviruses and bacteriophage), including, but not limited to pets, such as dogs, cats, and birds; farm animals such as pigs, cattle or cows, goats, chickens, ducks, turkey, and sheep, as well as other animals, such as apes, bison, camels, horses (for example, racehorses, such as Harness and Thoroughbred), whales and dolphins. Genetic profiles may also be generated for plants, including but not limited to commercially important plants such as, for example, agricultural plants including but not limited to cotton plants, olive trees, evergreen coniferous trees, banana trees, apple trees, orange trees, grapefruit trees, cherry trees, almond trees, wheat, corn, hemp, soybeans and rice. Genetic profiles can be generated for fish, including but not limited to salmon, tuna, sea bass, Alaska pollock, cod, eels, tilapia, flashlight fish, anglerfish, *Kryptophanaron alfredi*, or sharks. Genetic profiles can also be generated for invertebrates, such as lobsters, shrimp, scallops, *Tomopteris* and insects; microorganisms, such as bacteria or viruses; and endangered species or extinct species from which genetic material can be obtained.

[00291] For example, phenotypes that may be tested for in non-human animal's may be coat color(s), eye color, nose color, size, temperament, intelligence, agility, speed, racing performance, performance at conformation events, amount of shedding, amount of milk production, percentage of protein in milk, percentage of fat in milk, muscle strength, amount of lean meat, height, weight, eye color, longevity, reproductive capacity, and diseases and disease susceptibility, such as hip dysplasia, exercise-induced collapse or colic. Initial and reflex phenotypes may be determined based on an agricultural company's, government's, farmer's, animal trainer's, veterinarian's, or pet owner's (or prospective pet owner's) preference. For example, a prospective pet owner may value a dog's coat color or performance at conformation events first, and thus have an initial phenotype for coat color, performance at conformation events, or both. If, for example, the predisposition for a puppy's grown size fits the prospective pet owner's size restriction, reflex testing to the prospective pet owner's second criteria, such as intelligence or exercise induced collapse, is performed. If the puppy does not fit the prospective owner's size restriction, no reflex testing may be performed. Additional rounds of reflex testing may be performed.

[00292] Reflex testing can apply to both actual testing of the genotype (e.g., laboratory genetic test), the analysis of the genotype, and/or the reporting of the genotype or phenotype or both. Reflex testing may also apply to only genotype testing and analysis or to only reporting of the genotype or phenotype or both. For example, reflex testing may mean that actual testing (genotyping) for those genetic variants is not conducted until a risk or predisposition or carrier status or diagnosis for the first phenotype, such as a disease or trait or process, is genotyped or before the risk or predisposition or carrier status or diagnosis for the first phenotype, such as a disease, is ascertained. Reflex testing may also mean that genotyping for the reflex phenotype, such as a disease, condition, trait or process, occurs either before or after or at the same time of the genotyping for the first disease or trait or process but the results are not reported (such as not entered into any genetic analysis algorithms or analyzed or being shown anywhere in the report for an organism's genetic profile or conveyed in any manner to the organism or entity that ordered the genetic profile, or who views or has access to the results) unless there is an increased or decreased predisposition or carrier status identified for the first phenotype. Reflex testing also applies to the physical testing and genotyping process, the analysis of the genotypes and phenotypes as well as using or conveying the results (whether genotypes or phenotypes or predisposition or carrier status or diagnosis or any or all of the above) by electronic means, by paper, in-person, by verbal means, or any other means, to the entity, person, information technology system, or analytical program that is conducting the testing or analysis, or both, as well as the person that ordered the test, views or has access to the test, as well as using the genotypes or phenotypes or predispositions for or in any analysis or interpretation of the raw or analyzed genotype data or any other genotypes or phenotypes or predispositions. This means that reflex testing is not time dependent upon when the initial genetic testing (the actual genotyping) is conducted and is also not dependent upon when the initial phenotype or panel's first round (before any reflex testing) of analysis for risk or predisposition or carrier status is conducted. Reflex testing may occur immediately following the diagnosis of a phenotype or the genetic testing (the actual genotyping), the initial analysis for the phenotype or panel or both (before any reflex testing is conducted), or at any other time point in the future, such as seconds, minutes, hours, days, weeks, months, years, or decades after either the initial genetic testing (the actual genotyping) or the initial analysis or both is conducted. Therefore, an organism may find that they are either genetically predisposed to coronary artery disease or have been diagnosed with coronary artery disease at earlier Time A, but then at a later time, Time B, either the organism, their healthcare provider, such as an Internist or Cardiologist or Pharmacist, or a third party, may want to analyze, deduce, investigate, ascertain or find out the organism's genetic risk or predisposition to adverse reactions to HMG-CoA reductase inhibitors (Statins). If genetic testing (actual genotyping) or genetic analysis (of genotypic data) or both is then conducted to ascertain the organism's risk or predisposition to adverse reactions from HMG-CoA reductase inhibitor medication at the later Time B, because it is known from earlier Time A that the person is predisposed to coronary artery disease or because the person is diagnosed with coronary

artery disease, or both, then this also constitutes reflex testing. As stated, reflex testing may occur immediately, or any time in the future, such as seconds, minutes, hours, days, weeks, months, years or decades after one or more of the following: the initial genetic testing (actual genotyping) is conducted or diagnosis of the phenotype is made or predisposition or risk or carrier status for the phenotype is ascertained (through genetic analysis of the genotypic data).

[00293] Reflex testing can also be accomplished either on the front end or back end of the analytical or reporting process or both. For example, if an organism has an increased predisposition for obesity, or has a high body mass index, then the reflex may analyze or show the person's predisposition to diabetes mellitus, type II (diabetes). Reflex testing may work by the analytical process identifying that an increased predisposition for obesity is present (predisposition can either be increased chance of getting the phenotype or decreased chance of getting the phenotype or being a carrier of the phenotype, which means that the person either carries or has or likely has the phenotype) and therefore reflexes to showing predisposition for diabetes. Diabetes predisposition may only be shown if a person is found to be at increased or decreased predisposition or a carrier for obesity. If the person is not found to be at increased or decreased predisposition or a carrier for obesity, then diabetes predisposition may not appear in the report for the organism's genetic profile. This constitutes 'front-end' reflex. Alternatively, reflex testing could occur by the analytical process identifying (i.e. calculating from the alleles or genotype(s) of one or more genetic variants) both predisposition for obesity (either increased or decreased predisposition or carrier status) and predisposition for diabetes (either increased or decreased predisposition). If there is an increased or decreased predisposition or carrier for obesity then no change is made and the predisposition for diabetes is included in the analysis and is included in the genetic report. However, if no increased or decreased predisposition or carrier for obesity is found then the predisposition for diabetes is covered up (greyed out; blacked out; ignored; deleted; not shown, reported, or provided; made to appear less relevant or irrelevant; or such) and is either not displayed further in the analysis or the genetic report or both or is moved to the back of the genetic report, or otherwise made less relevant or irrelevant in the genetic reporting process, such as by putting it in a separate section of the report or conveying those results in a less relevant manner to the organism, such as by placing that information in a less relevant section of the genetic report, such as in a less relevant section of a webpage or website (for example, not placing the reflex phenotype information in the main or primary or same section where risk or predisposition or carrier status or diagnosis pertaining to the initial phenotype or the relevant phenotypes or the phenotypes found associated with either higher or lower risk is presented). This constitutes 'back-end' reflex testing.

[00294] In some embodiments, reflex testing is based on a predisposition or risk to a phenotype (e.g., disease, disorder, trait or condition). However, in some embodiments, reflex testing is not based on predisposition as some genetic variants are deterministic of disease, therefore reflex testing can be predicated upon an organism having a single genetic variant that is either deterministic for a

phenotype (the organism either is a carrier but not affected by the phenotype or has or likely has the phenotype) or is associated with either increased or decreased predisposition for a phenotype. For instance, an organism may be found to carry a genetic variant that causes (is deterministic for) cystic fibrosis. If this occurs, then reflex testing may occur that will look at other genetic variants in order to ascertain degree of lung disease with cystic fibrosis, severity of cystic fibrosis and prognosis with cystic fibrosis.

[00295] In some embodiments, reflex testing is based on a phenotype that is not determined by genotyping or genetic analysis. For example, a medical history, or a diagnosis may indicate a phenotype such as for example cancer, or obesity or any of the phenotypes provided herein. The indicated phenotype may then cause another phenotype to be genotyped or not genotyped, to be analyzed or not to be analyzed, to be included in the report or not to be included in the report, to be included in a specific section of the report or not to be included in a specific section of the report, or any combination thereof.

[00296] The reflex phenotype may or may not be included in the raw data or as part of the preliminary analysis but its inclusion in the near-final and final report that is delivered to the organism, the health-care provider, or any third-party who ordered the test is determined by whether or not there is a diagnosis, carrier status or an increased or decreased predisposition of the first phenotype, or whether a specific milestone event (trigger event) has occurred (as discussed previously). As reflex testing can go through multiple rounds and multiple layers deep (for example, first phenotype reflexes to second phenotype that reflexes to third phenotype that reflexes to fourth phenotype, etc.), this is applicable to each and every step. For instance, if reflex testing is indicated (either by one or more deterministic genetic variants (carrier) or by an increased or decreased predisposition for or a diagnosis of a phenotype) for the second phenotype, which is also found to be increased risk and this causes reflex testing for a third phenotype. As an example, if a person is found to be predisposed to obesity then reflex testing may occur to round 2 to discern the person's predisposition for diabetes and if the person is predisposed to diabetes then reflex testing may continue on to round 3 to discern the age of onset of diabetes and if the person has a predisposition for greater or less effectiveness of or adverse reactions to any medications that are used to treat pre-diabetes or diabetes.

[00297] Reflex testing of the second phenotype may cause the analysis or reporting of the first phenotype to be modified. For instance, if a deterministic genetic variant for Hemochromatosis is found and reflex testing shows that other genetic variants indicate that Hemochromatosis may be severe, then the report may indicate this (that the person has a genetic variant that is associated with Hemochromatosis and that the disease presentation may be severe). The reflex testing may also cause both phenotypes to not be reported. An increased predisposition for a disease may be ascertained based on the allele or genotype of one or more genetic variants. This may cause reflex testing of an associated phenotype that negates the first phenotype. For example, the disease Hemochromatosis may be found initially but reflex testing may examine and analyze other genetic variants that may be

associated with either very low or no penetrance or expressivity of Hemochromatosis for that organism. Therefore, neither Hemochromatosis nor the reflex testing results, or both, may be included anywhere in the analysis or Genetic Report or, alternatively, they may both be included in the report, such as in the main section or in a different section. Both phenotypes also may both be included in the raw analytic data, one may be included in the raw analytic data, or neither of the phenotypes may be included in the raw analytic data.

[00298] Reflex testing may take into account many different factors besides the genotype of one or more genetic variants. These non-genotype factors may either occur at the first step or at a later step (such as where risk of uterine cancer is deduced but the reflex to medical history shows the organism had a hysterectomy and therefore the risk of uterine cancer is not included in the analysis of the organ system or in the analysis of the entire genetic health of the organism and may or may not be included in report).

[00299] The risk for the reflex phenotype may be tested at the same time as the initial phenotype; for example, a single sample may be used to test both the initial phenotype and the reflex phenotype. Alternatively, the reflex phenotype may be tested after the initial phenotype, and another sample used, or perhaps an aliquot of the initial sample that was stored may be used. The reflex phenotype and the initial phenotype may be tested at the same time, and the results for each test may be analyzed at the same time. Alternatively, the reflex phenotype and the initial phenotype may be tested at the same time, and the results analyzed at different times. For example, if the initial phenotype produces a positive result, the results for the reflex phenotype may be then analyzed. The reflex phenotype can be reported concurrently with the initial phenotype, or subsequent to the initial phenotype. The reflex phenotype can be initially requested by the organism, or third party, or after the organism receives the results of the initial phenotype, and optionally, after consultation with a genetic counselor, physician, nurse practitioner, physician assistant, other healthcare provider, or third party. The reflex phenotype(s) may cost additional fees.

[00300] The panels described herein are used for determining the risk or predisposition of at least 2 phenotypes, which may include 2 phenotypes in the initial round of analysis or 1 phenotype in the initial round of analysis and 1 or more phenotypes deduced via reflex testing. The phenotypes may be monogenic, multigenic, or multifactorial and each phenotype may be associated with one or more of the following: monogenic, polygenic, or multifactorial genetic variant(s). The panels can be used for determining the risk or predisposition of 1, 2, 3, 4, 5 or more multifactorial phenotypes alone or 1, 2, 3, 4, 5 or more monogenic phenotypes alone or both 1, 2, 3, 4, 5 or more multifactorial and 1, 2, 3, 4, 5 or more monogenic phenotypes. The multifactorial and monogenic phenotypes can be tested for and analyzed together, either at the time the initial genetic testing is conducted or at any other time based on genetic testing data (the detection of genetic variants via arrays, microarrays, massarrays, beadarrays, PCR, from partial or full exome or partial or full genome sequencing, such as with

nanopore sequencing, or any other methodology that allows for the detection or identification of genetic variants throughout a genome).

[00301] A panel can be premade and presented to the organism, entity or third party ordering the genetic testing or genetic analysis or both, or the panel can be chosen at the time of consultation from a list of phenotypes that may be grouped according to organ system, disease process, age of onset, clinical relevancy, habits relevancy or any other grouping. The list of phenotypes may appear on a laboratory requisition form. The list may be in alphabetical order or grouped according to organ system, medical specialty, disease process, age of onset, clinical relevancy, habits relevancy or any other grouping. An organism, entity, or third party ordering the genetic testing or genetic analysis or both may then choose a subset of these phenotypes such that a panel is constituted by a group of 2, 3, 4, 5, 6, 7, 8, 9, 10 or more phenotypes, or up to 10, 20, 25, 30, 35, 40, 45, 50, 100, 200, 300, 400, 500, or 1000 phenotypes.. Organisms may also choose other options. These phenotypes may then either be tested for or, if the raw genetic data already exists, then the genetic analysis may be conducted and all applicable reflex testing conducted for these phenotypes, taking into account each of the phenotypes selected both organismly and in-relation to each other, and a genetic report can be produced.

[00302] The panels (also referred to as genetic testing panel or a genetic panel, and other variations thereof) can be defined as any group of two or more phenotypes reported together at any time, regardless of when the genetic testing (the actual genotyping) occurred. For example, a fetus or newborn may undergo full genome sequencing so that in part or substantially the entire genetic code is obtained at that time. The phenotype information that is then analyzed or conveyed in a report, or medical record, can constitute a panel. The analysis, reporting or both, of the phenotypes in regards to being designated a panel is not time-dependent in relation to when the genetic testing (genotyping) occurred. The analysis, reporting, or both, can occur at any time, for example, during the initial genotyping (such as sequencing) or at any later date, such as seconds, minutes, hours, days, weeks, months, years or decades later, and the analysis, reporting or both of the phenotypes at any point of time still constitutes a panel. For example, the phenotype(s) may be determined initially, at approximately the same timeframe as the obtaining of genetic data, or may be determined later, or a combination thereof, such that some phenotypes are determined initially and some phenotypes are determined at a later time.

[00303] Any genetic variant-phenotype associations or phenotypes based on genetic information that is analyzed or reported together as a group, or both, constitutes a panel. This allows for genetic sequence information containing genetic variant information to be stored in a database or other device or medical record and to be analyzed either at that time or at a later date, such as when the information, such as clinical information, may be more pertinent or useful to a medical professional, or both. Panels and/or reflex testing and/or OP-CADI may also be ordered by and are applicable to patients, clinicians, veterinarian or veterinary surgeon, pet owners, animal owners, pharmacists,

healthcare providers, insurance companies, hospitals, clinics, academic researchers, laboratory researchers, clinical researchers, pharmaceutical companies, agricultural companies, agricultural managers, ranchers, farmers, military personnel, governmental agencies, local, national and international agencies, such as the United States Food and Drug Administration (FDA), European Union (EU), United States Centers for Disease Control (CDC), United Nation's World Health Organization (WHO), World Organisation for Animal Health (OIE), United Nation's Food and the Agriculture Organization (FAO), or any entity that may be interested in or able to utilize genetic information.

[00304] The panels described herein, and subsets thereof, may be used for a variety of applications and in a wide range of settings. Similarly, a wide range of persons may request a genetic test. For example, the organism to be tested, an organism seeking to confirm paternity, an organism's owner or representative or third party seeking information about potential sperm or egg donors or about the actual sperm or egg or embryo itself, or other governmental agency or subagencies or related agencies such as the Secret Service, the Department of Defense (DoD), the Defense Advanced Research Projects Agency (DARPA), Department of Homeland Security (DHS), Department of Agriculture (DoA), the White House, the Federal Bureau of Investigation (FBI), the National Security Agency (NSA), the Bureau of Alcohol, Tobacco, Firearms and Explosives (ATF), the Central Intelligence Agency (CIA), the National Reconnaissance Office (NRO), the Joint Special Operations Command (JSOC), the Defense Intelligence Agency (DIA), the Bureau of Intelligence and Research (INR), the Office of Intelligence and Counterintelligence, the Drug Enforcement Administration (DEA), National Aeronautics and Space Administration (NASA), or international agencies such as North Atlantic Treaty Organization (NATO), the United Nations (UN) and the UN Security Council, or any other government or governmental agency of any country or collaboration of countries, such as the Secret Intelligence Service (SIS) and MI6, the Defence Intelligence Staff (DIS), the HaMossad leModi'in uleTafkidim Meyuhadim (Mossad), the Canadian Security Intelligence Service (CSIS), the Bundesnachrichtendienst (BND), the Naikaku Jōhō Chōsashitsu (Naichō), the Militaire Inlichtingen-en Veiligheidsdienst (MIVD), the Nasjonal sikkerhetsmyndighet (NSM), the Inter-Services Intelligence (ISI), the Federalnaya Sluzhba Bezopasnosti (FSB), the Re'asat Al Istikhabarat Al A'amah (GIP), the Security and Intelligence Division (SID), the Indian Space Research Organisation (ISRO), the National Directorate of Security (NDS), the Centro Nacional de Inteligencia (CNI), the National Security Bureau (NSB), the Directorate-General for External Security, the National Intelligence Service (NIS), or any other governmental organization or agency, as well as aerospace, defense, or advanced technology companies such as Lockheed Martin, Raytheon Company, or Northrop Grumman Corporation, or private security companies or private military companies (PMCs), such as Blackwater Worldwide, ArmorGroup International PLC, Hart Security, Military Professional Resources Inc. (MPRI), or Pacific Architects and Engineers, or other third party, as well as an employer or potential employer, an insurance company, or other third party.

[00305] An organism's owner who has received certain results from a medical examination or medical test may also be tested with a specific panel, or subset thereof. One or more panels, or subsets thereof, may be selected based on the medications or supplements (e.g., vitamins, herbal supplements, minerals) an organism is taking or considering taking or may take in their future. A panel, or subset thereof, may also be used to test an organism that has a particular habit or possesses specific phenotypes, such as trait(s), or wants to find out if they or their current or future children have or may have specific phenotypes, such as traits.

[00306] Breeders, ranchers, herders, owner's, and/or potential owners, that may be interested in the panels may be those interested in an organism's future offspring's genetic profile and phenotypes. Such organisms can have a genetic profile determined from the combined analysis of the offspring's prospective parents. The method is referred herein as "offspring projections from the combined analysis of different organisms", or OP-CADI (see **FIG. 14** and **FIG.21**). The genetic profile of each of the organism's parents is first organismly analyzed and then combined. Thus, provided herein is a method of utilizing the genotypic and phenotypic information from these two organisms to view potential genetic profiles of their potential future offspring by comparing phenotypes, genes, loci, genetic variants, as well as carrier status and the odds ratios or other risk values attributed to each genetic variant, in order to ascertain the future offspring's lifetime risk ranges for the phenotypes and carrier status of phenotypes. OP-CADI can be applicable to a single genetic variant, a single gene, a single locus, a single phenotype, part of the genome or the entire genome and may take into account monogenic, polygenic, and/or multifactorial phenotypes, as well as potential or suspected non-genetic factors that the offspring may be exposed to or interact with.

[00307] For example in humans, the female's genetic profile may be found to have genetic variants associated with Epidermolysis Bullosa Simplex, Cystic Fibrosis, Alzheimer's Disease, Macular Degeneration and being an Endurance Athlete while the male's genetic profile may be found to have genetic variants associated with Prostate Cancer, Cystic Fibrosis, Androgenic Alopecia, Alzheimer's Disease, and being an Endurance Athlete. The future child's genetic profile and analysis may contain the following information: Epidermolysis Bullosa Simplex – 25% chance of being a carrier, 75% chance of being a non-carrier, Cystic Fibrosis – 25% chance of being affected, 50% chance of being a carrier, 25% chance of being a non-carrier (neither affected nor a carrier), Alzheimer's Disease – Predictive Medicine Lifetime Risk Range 23-45%. Macular Degeneration – Predictive Medicine Lifetime Risk Range 15-25%. Androgenic Alopecia – Predictive Medicine Lifetime Risk Range 5-25%, Prostate Cancer – Predictive Medicine Lifetime Risk Range 14-22%, Endurance Athlete – Very high probability of having this trait, such as greater than 75% chance.

[00308] Couples interested in having children using their own genetic material, or by assisted reproductive technologies, such as by showing the potential genetic profile of offspring from an egg donor or sperm donor or both, may use OP-CADI. Breeders of livestock and other animals, animal researchers, and organisms, researchers, or companies working with animals, mammals, fish, birds,

reptiles or plants may also utilize OP-CADI in order to ascertain the projected phenotypes from different mate pairings, and they may base their mate selection on results that show either an increased likelihood of one or more phenotypes or a decrease likelihood of one or more phenotypes, or an increased likelihood of one or more genetic variants or genes or loci or a decreased likelihood of one or more genetic variants or genes or loci, and/or the carrier status of one or more phenotypes, from the OP-CADI results from one or more mate pairings analyzed. OP-CADI may also allow for genetic information from genetic testing on a number (from 1 to over 1,000,000,000) of both potential male and female parents to be analyzed together and to create mate pairs that are more likely to produce one or more genotypes and/or phenotypes, or that are less likely to produce one or more genotypes and/or phenotypes, or a combination of the two (some genotypes and/or phenotypes are more likely while other genotypes and/or phenotypes are less likely, with one or more of the following: monogenic, polygenic, or multifactorial phenotypes). OP-CADI is applicable to all species, including human and non-human, that produce offspring through the combination of genetic material from two parents. Also provided herein are methods for matchmakers and matchmaking services to use this method for matching organisms based on their genetic profiles or the genetic profiles of their potential children or both.

[00309] The OP-CADI takes into account the fact that offspring inherits approximately 50% of their autosomal genetic code from one parent and 50% from the other parent. At the same time, male children typically have a 100% chance of inheriting their y-chromosome from their father and females typically have a 100% of inheriting the one X-chromosome that the father has. At the same time, both male and female children typically have a 100% chance of inheriting the mitochondrial genetic code from their mother.

[00310] By analyzing the respective genetic codes of both parents, projections can be made about the potential genetic code and the potential phenotypes of their offspring. Monogenic diseases follow Mendelian inheritance patterns (see for example, **FIG. 2**), and penetrance and expressivity may be determined through published data on the specific genetic variant(s), the gene, or the phenotype, such as the disease, and through an analysis of the genetic sequence and genetic variants that the parents' genomes contain. Thus, the chance of a child being affected with a phenotype, being a carrier of a phenotype, or being neither affected nor a carrier (a non-carrier), also known as their carrier status, as well as being at increased risk for a phenotype or decreased risk for a phenotype, can be deduced and this information can then be supplied to the organism interested in having the potential offspring or their physician or veterinarian or veterinary surgeon or agricultural manager or agricultural company or rancher or farmer or other third party. Polygenic and multifactorial disease risk is determined by calculating the AS, CAS, CGR or PMR (as described herein), but OP-CADI combines both the potential father and potential mother's genetic profile in order to project or predict the genotypes and phenotypes of their potential offspring. The father most often contributes ~50% of his autosomal genetic code, 100% of his y-chromosome code to any sons and 100% of his x-chromosome code to

any daughters while the mother most often contributes ~50% of her autosomal genetic code, one of her two X-chromosomes to any daughters, and 100% of her mitochondrial DNA to their offspring.

[00311] For the autosomal genetic code, in some embodiments, the first step in the analytical process is for a manual operator or the genetic analysis information technology system to perform multiple 'chops', with each chop taking into consideration approximately 50% of all the genetic variants that make the cut-off (such as $GVDC \geq 1.5$) for each phenotype being accessed (determined by the genetic variant(s), gene(s), locus, or phenotype(s) or panel(s) chosen for analysis) in order to determine the lowest possible lifetime risk and the highest possible lifetime risk for each polygenic or multifactorial phenotype. Therefore, OP-CADI analyzes all relevant genetic variants throughout the entire genome (that make the cut-off) in-relation to each phenotype. This is done separately for the female parent and for the male parent. The genetic profile chop for the female parent containing the genetic variants that constitute the lowest lifetime risk for each phenotype being assessed is designated "Mother – Low" and the genetic profile chop for the female parent containing the genetic variants that constitute the highest lifetime risk for each phenotype being assessed is designated "Mother – High". The genetic profile chop for the male parent containing the genetic variants that constitute the lowest lifetime risk for each phenotype being assessed is designated "Father – Low" and the genetic profile chop for the male parent containing the genetic variants that constitute the highest lifetime risk for each phenotype being assessed is designated "Father – High". Monogenic disorders generally follow monogenic Mendelian inheritance patterns for genes and genetic variants located on autosomes. Once the set of genetic variants that constitute the lowest lifetime risk and the highest lifetime risk for each phenotype being accessed has been deduced, these final-chop profiles from the female and male are merged, as described below.

[00312] Genetic variants that exist close to each other on the same chromosome are more likely to be inherited together, and therefore different chops are also made taking into account different measures of linkage disequilibrium, such as a chop when the $r^2 \geq 0.5$, $r^2 \geq 0.75$, or $r^2 \geq 0.90$ in order to discern the changes in the risk values (such as the predictive risk values) obtained if these genetic variants are inherited together or if they are not, along with the chances that they will be inherited together or that they won't be inherited together based on their r^2 or D values. All genetic variants with a $r^2 \geq 0.99$ may be analyzed as being inherited together and may not be separated (separated meaning that the two genetic variants may be analyzed as potentially being separated during the inheritance process simulated by each chop, such as for example that one genetic variant is inherited while the other genetic variant is not) during the chop process. Alternatively, it may be designated that all genetic variants with a $r^2 \geq 0.95$ or any operator-designated r^2 cut off value may be chosen so that any two or more genetic variants with an r^2 below that threshold may be separated during the chop process and any two or more genetic variants with r^2 above the designated threshold will be analyzed as being inherited together (meaning that they may not be separated during the chop process).

[00313] For the sex chromosomes (for example, the X- and Y-chromosomes in *Homo sapiens sapiens*) genetic code, for the female parent, 50% of all the genetic variants from her X-chromosomes for each phenotype being assessed from her are analyzed within each chop. The genetic variants that constitute the lowest lifetime risk for each polygenic or multifactorial phenotype is combined within “Mother – Low” genetic profile and the genetic variants from the chops that constitute the highest lifetime risk for each phenotype are combined within “Mother – High”. This is applicable to both the potential female and male offspring. For the male parent, approximately 100% of the genetic variants from his single X-chromosome is combined into “Child – Low” and also “Child – High” for the potential female children. For potential male children, approximately 100% of the genetic variants from his (the male parent’s) single Y-chromosome are combined into “Child – Low” and also “Child – High”. Monogenic phenotypes, such as disorders, may follow monogenic Mendelian inheritance patterns or sex-linked inheritance patterns for genes and genetic variants located on sex chromosomes. For species other than human, known species-specific inheritance patterns for each chromosome from each parent can be utilized in a similar way in order to conduct the OP-CADI for any species where the genetic material of the offspring is from the combination of genetic material from two parent organisms.

[00314] For the mitochondrial genetic code, all offspring (e.g. children) are expected to inherit 100% of the mitochondrial genetic code from the female parent. Because of this, the analysis of the mitochondrial genetic code for “Child – Low” and “Child – High” (described below) utilizes 100% of the mitochondrial genetic code from the female parent. Sometimes genetic variants from the autosomes or sex chromosomes or both are analyzed together with mitochondrial genetic variants in the determination of carrier status or risk of certain phenotypes (for instance, in the analysis of the ‘Exercise Intolerance’ as well as the ‘Deafness’ phenotypes). In this case, the OP-CADI analysis takes into consideration all of the female parent’s mitochondrial genetic variants for those phenotypes being assessed and ignores the male parent’s mitochondrial genetic variants.

[00315] This merger involves two parts, as shown in **FIG. 14**. Part 1 involves taking the genetic variants that constitute the lowest lifetime risk for a phenotype from the female parent (Mother – Low) and combining them with the genetic variants that constitute the lowest lifetime risk for a phenotype from the male parent (Father – Low). This new genetic profile is designated “Child - Low” and all the genetic variants (now a combination containing approximately 50% from the male parent and approximately 50% from the female parent) are run again through the genetic analysis system in order to arrive at the lowest lifetime risk value possibility for the possible offspring of these two parents. Part 2 involves taking the genetic variants that constitute the highest lifetime risk for a phenotype from the female parent (Mother – High) and combining them with the genetic variants that constitute the highest lifetime risk for a phenotype from the male parent (Father – High). This new genetic profile is designated “Child - High” and all the genetic variants (now a combination containing approximately 50% from the male parent and approximately 50% from the female parent)

are run again through the genetic analysis system in order to arrive at the highest lifetime risk value possibility for the possible offspring of these two parents. Combining the lifetime risk values ascertained for Child - Low and the Child - High gives a range, with the lowest value possibility being the value for Child -Low and the highest value possibility being the value for Child -High. This constitutes the lowest lifetime risk and carrier status and highest lifetime risk possibilities and carrier status (the "Child - Range") for one or more phenotypes for any potential offspring.

[00316] Taking into account the fact that X-inactivation will typically occur in any mammalian female offspring, the OP-CADI gives the range of possibilities. The potential genetic profiles of mammalian female children (Child – Low and Child – High) primarily looks at a mosaicism pattern and therefore considers the two X-chromosomes (the one paternally derived X-chromosome and one of the X-chromosomes from the female parent, as well as repeating the steps of the analysis, this time with the same paternally derived X-chromosome but now with the other maternally derived X-chromosome) no different from the autosomes in the analysis in terms of finding the lowest range value and highest range value and the most likely outcome existing within this range. In some embodiments, this can be accomplished by assessing the phenotypes if the X-chromosome from their father is inactivated and then another assessment where the X-chromosome from their mother is inactivated. However, the mosaicism pattern created due to lyonization is also taken into account by determining the carrier status and risks of phenotypes when one X-chromosome is inactivated versus when the other X-chromosome is inactivated, and these different chops of examining and predicting lyonization results, may provide for a different, and potentially more accurate range for the potential female children. Similarly, the potential for crossing-over between the paternally derived X-chromosome and the maternally derived X-chromosomes' pseudoautosomal regions may be considered when assessing phenotypes associated with one or more genetic variants on one or more sex chromosomes. Inheritance laws surrounding X-inactivation may be species specific and are known to persons of ordinary skill in the genetic analysis arts, and are integrated into the OP-CADI algorithm. For example, X-inactivation in marsupials occurs only to the paternally derived X-chromosome and therefore marsupial OP-CADI will analyze the potential offspring with the paternally derived X-chromosome inactivated (and the maternally derived X-chromosome will not be inactivated), meaning that the genetic variants and their associated phenotypes on the paternally derived X-chromosome may not affect the offspring and may not appear in the analysis and/or the report.

[00317] The OP-CADI can also give separate results for a potential female offspring (such as a child) and a potential male offspring (such as a child), and thus a separate OP-CADI Genetic Report can be generated for the potential female offspring (such as children) and the potential male offspring (such as children). The primary difference occurs with whether the male parent's X-chromosome is considered in the analysis (for all female children) or whether the male parent's Y-chromosome is considered (for all male children). The offspring are separated by gender, so that OP-CADI can give risk and carrier status information about the potential female offspring and about the potential male

offspring. It may be that the male offspring has a significantly higher risk or has an affected carrier status of a harmful phenotype, such as if it is an x-linked disease, and thus the male offspring and female offspring's OP-CADI report may be different. Based on this information and analysis, mate pairing and possible sex selection methods can then be utilized, such as sperm sorting, pre-implantation genetic diagnosis and prenatal diagnosis, in order to choose or increase (or decrease) the likelihood of any phenotype(s), such as of gender, or of any genetic variant(s), gene(s), genetic sequence(s), or chromosome(s).

[00318] The above methodology can also be used for polygenic, multifactorial and/or monogenic phenotypes. For example, for monogenic phenotypes, probabilities of a phenotype may be given. For instance, if humans if both parents are carriers of a genetic variant in the CFTR gene associated with the cystic fibrosis phenotype, then the probability of their child being affected with cystic fibrosis is 25%, the probability of the child being a carrier of a genetic variant associated with cystic fibrosis is 50%, and the probability of the child being neither affected nor a carrier (a non-carrier) is 25%. This type of probability deduction follows the tenants of monogenic Mendelian inheritance (see for example **FIG. 3**).

[00319] Multifactorial phenotypes (that take into interactions between one or more genetic variants and the environment), may be treated as polygenic. However, the OP-CADI Genetic Report for the offspring, such as children, may contain information relating to how non-genetic factors may influence the risk of certain phenotypes. By supplying this information to the parents, the parents can recognize how different non-genetic factors may influence their potential children. Alternatively, the OP-CADI may take into account non-genetic factors, such as if it is known that the offspring will live in an urban environment or if it is known that the offspring will be farm-raised, or raised for a specific function, such as equine raised for Thoroughbred or Harness racing. These non-genetic inputs for multifactorial phenotypes may then be utilized during the OP-CADI analysis so that the analysis and results may be interpreted with these non-genetic factors as well.

[00320] Genomic imprinting applies to certain phenotypes when the phenotypes only arise, or have a greater or lesser probability of arising, when the gene (containing the genetic variant(s)) is inherited from a specific parent (such if a phenotype only manifests if the genetic variant is inherited from the mother, while if it comes from the father than there is either a different phenotype or no discernable phenotype, and vice versa). Genomic imprinting, regarding phenotypes for which this is known to apply, is taken into account during the analysis process with the OP-CADI. For example, the diseases Prader-Willi Syndrome and Angelman Syndrome both are determined via parent-of-origin genomic imprinting. For genetic variants that are associated with these diseases, if the genetic variant comes from the female parent's genetic code then the probability of disease relates to Angelman Syndrome but if the genetic variant comes from the male parent's genetic code than the probability of disease relates to Prader-Willi Syndrome. Genomic imprinting relates not only to monogenic diseases but also to polygenic and multifactorial diseases. For example, atopy, atopic dermatitis and asthma have

all been associated with genetic variants in the SPINK5 gene, but only when those genetic variants are maternally inherited. (Walley *et al. Nat Genet* 29(2): 175-178 (2001)). Probabilities and risk-ranges of some phenotypes depend on which parent is contributing the genetic variants (as ascertained from published literature) and this is taken into account with the OP-CADI.

[00321] The OP-CADI may also be used for parent selection (mate selection) purposes, such as when choosing either a female egg donor or male sperm donor or both. For example, if a married couple is unable to have children because the female has fertility issues, the couple may choose to search for an egg donor while planning to utilize the husband's sperm in order to fertilize the egg. The OP-CADI can be used as a scanning methodology that utilizes the husband's genetic profile and combines it with an egg donor's profile in order to assess the possible genotypes and phenotypes of the potential children. This process can be run for all possible egg donors under consideration, either one at a time, in batches of egg donors, such as 2 or 5 or 10 at once, or by utilizing the genotypic information available from all egg donors at once.. If the genetic profile (genotype, such as for example via genechip analysis, PCR analysis, or sequencing) of the egg donors has already been deduced, then this process may be run automatically back-to-back or simultaneously until a certain genotype or phenotype probability or risk-range or carrier status is deduced. For example, the couple may want to ensure that the potential child will have the lowest risk-range of breast cancer possible, then the OP-CADI can be utilized to scan the available egg donor's genetic profiles in-order to ascertain which egg donor(s) will provide the lowest risk-range for breast cancer both on its own and when combined with the male parent's genetic profile. This approach can be utilized for any phenotype, and can be utilized for either just one phenotype or multiple phenotypes (for example in terms of humans, the lowest probability for all rare diseases and the lowest risk-range for breast cancer, Alzheimer's disease, and heart disease as well as the highest probability or highest risk-range for enhanced longevity, intelligence and blond hair). The above process can be utilized for any parent selection purpose that wants to take into account the genetic profile of the potential children. For example, it may also be utilized by a woman who wants to discern who the best sperm donor(s) will be based on certain cut-offs that they impose upon the potential future children's genetic profile (for example, less than (<) 25% probability of any rare disease, metabolic disease, or syndrome).

[00322] A similar process may also be used by matchmakers or matchmaking services such that organisms submit their DNA or genetic profile and the matchmaker or service uses the OP-CADI to determine the potential genetic profiles for each match's potential children. Based on cut-off values supplied by either the matchmaking service for the organisms themselves (such as all matches must have less than (<) 25% probability of rare diseases), organisms can then be matched up. This information may also be combined with other analysis of each of the organisms own genetic profiles, for example to determine compatibility based on degree of sexual responsiveness. This constitutes a comprehensive analysis of all available genetic information in-order to try to ascertain the most appropriate or best matches on a genetic level set by certain cut-offs that are either determined by the

matchmaker, the matchmaking service, or the organisms themselves. This may further be combined with each organism's personal preferences (such as preference for the other person's hair color or education level) in order to arrive at matches that are matched based on both genetic and personal preference factors.

[00323] The above process for the OP-CADI refers to genetic data ascertained through any method. For example, genetic data may be from array testing or nanopores or any other techniques that may not identify which specific chromosome that the genetic variant is from. For gene sequencing, full exome sequencing and full genome sequencing, each organism chromosome may be seen as a discrete entity. The information pertaining to which specific chromosome a genetic variant is contained on can be utilized within the analysis in order to identify a string (two or more) genetic variants that are likely to be inherited together as those genetic variants occur close to each other on the same chromosome. A string of genetic variants may represent a haplotype or multiple haplotypes or it may just represent two genetic variants that are within physical proximity to each other on the same chromosome. Groups of genetic variants that exist closer together on the same chromosome may then move with more frequency together during each chop analysis. The effects of crossing-over may be taken into account and integrated into the OP-CADI by selecting a certain distance (such as in kilobases, or in centimorgans) that is more likely to segregate together. Genetic variants that exist on the same chromosome and within that certain distance from each other will then most likely segregate together and may not be separated during the chop process.

[00324] The OP-CADI can also be applied to non-humans, such as with the breeding of *Felis catus*, *Bos taurus*, *Gallus gallus*, *Pan troglodytes*, *Canis lupus familiaris*, *Capra hircus*, *Equus caballus*, *Mus musculus*, *Sus scrofa*, *Rattus norvegicus*, *Ovis aries*, *Meleagris gallopavo*, as well as other non-human mammals, aves or fish or plants. For example, the OP-CADI can be used to detect the pairs of canines (such as *Canis lupus familiaris*) that are most likely to produce offspring that are faster runners, have enhanced nighttime eyesight or have specific coat color. For bovine (such as *Bos Taurus*), this novel approach can be used to detect the pairs that are most likely to have more offspring, or offspring that are greater in size or produce larger amounts of milk. For species other than human, known species-specific inheritance patterns for each chromosome from each parent can be utilized in order to conduct the OP-CADI for any species where the genetic material of the offspring is from the combination of genetic material from two parent organisms.

[00325] The same process of genetic analysis applies to the OP-CADI as before, including applying the OP-CADI to any genetic variant(s), gene(s), locus, phenotype(s) or panel(s) and incorporating the option for reflex testing, which allows for a comprehensive, dynamic analysis of genetic information. The OP-CADI can utilize and report on lifetime risk-ranges and probabilities of genotypes or phenotypes or both, it can also be utilized and report on action score risk-ranges and probabilities of phenotypes, and it can also utilize and report on cumulative action score-ranges or genetic health

score ranges (such as existence score-ranges) and probabilities of phenotypes (such as for carrier status).

[00326] Any organism may be tested using one or more Full Genome Panel in order to determine his or her risk of, or predisposition for, one or more phenotypes. A full genome analysis panel may aid the calculation of the general health of the organism or of a zygote, embryo or fetus. An organism with a family history of a specific condition (e.g., acute disease, chronic disease, degenerative disease, fatal disease) may be tested with a full genome analysis panel. An organism on a particular diet may also be tested with such panel. In some cases, results from the Full Genome Panel(s) may help veterinarian or alternative professional make changes in the organism's habits (e.g., diet, exercise), or take actions to mitigate the organism's risk of developing an adverse condition. A full genome analysis panel may also be run on a fetal genetic material (such as from a zygote, embryo or fetus) or on newborns or children in-order to analyze and assess their entire genetic genome including phenotypes that may negatively or positively affect their life.

[00327] As is the case with the other panels described herein, if an organism is diagnosed with or tests positive (either increased or decreased risk as compared to the published gender-specific population generic lifetime risk for that phenotype as described herein) for a specific phenotype, such as a condition, within the Full Genome Panel (or subset thereof), one or more "reflex" phenotypes, such as conditions, may be tested. Knowledge gained from these tests may help the organism and/or their healthcare provider or third party plan an appropriate diet or, for example, limit his or her alcohol intake, or institute preventive measures and/or interventions to potentially minimize the impact of or avoid the diseases that the organism is found to be at increased risk for.

[00328] A panel may be used to determine an organism's Universal Identifier, which is a unique sequence of multiple genetic variants and the unique sequence at those variants when considered together is exactly specific to only one organism in the entire world. A Universal Identifier Option may be available for all panels that allows for a Universal Identifier to be added on to any panel for any organism or the Universal Identifier Option may be run on its own for any organism as its own Panel so that only a Universal Identifier is ascertained for the organism. This is similar to a fingerprint but is detectable in any specimen from the organism (e.g. blood, urine, hair, semen, skin, saliva, tissue, etc) that contains genetic material. This can be utilized either to confirm/verify identity (e.g., if meat is found to be tainted with E. coli or salmonella then it's Universal Identifier can be used to trace the meat back's entire history from a person's household or market all the way back through the entire distribution process to the ranch where the contaminated meat originated from) or for government and/or military use or for forensic use. For example, an organism's unique genotype at the genetic variants that constitute the Universal Identifier, can be used to identify or distinguish that organism from all other organisms in the world, with a probability of discrimination that may be greater than 90%, greater than about 95%, 99%, 99.9, or 99.99%. In some cases, the probability of discrimination may be greater than about 99.999, 99.9999, or 99.9999999999% or greater in all populations. The

Universal Identifier may be used on a variety of identification items such as on military identification tags (dog tags), on security cards, on documents, on medical records, on tissue specimens, on pathological specimens, on hair, blood, skin, saliva, semen or other bodily fluids, on stored genetic material, identification of organisms in government databases, in personal databases, in corporate databases, in military databases, in criminal databases, or any other use where personal identification with an extremely high degree of certainty and security are needed, wanted or required. This Universal Identifier may represent a minimum set of genetic variants necessary to distinguish one organism from all other organisms in the world out of all populations and therefore genotyping of only these genetic variants may be necessary to confirm, or to rapidly confirm, an organism's identity. This Universal Identifier may be composed of 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 20, 25, 30, 35, 40, 45, or 50 or more genetic variants throughout the organism's genome. The panel may also test for the organism's blood group based on specific genetic variants in multiple genes and this can be utilized to further confirm identity and also by healthcare professionals to confirm the organisms's exact blood group derived from other laboratory tests, such as another genetic way to further confirm identity or a confirmatory or ancillary indicator of blood group prior to a blood transfusion.

[00329] Because each organism has a unique universal genetic identifier (universal identifier), the identifier can be used to identify an organism, such as from the time of birth, so that the organism can be tracked throughout its life and also after its death, such as by a government agency, private or public company, veterinarian, herder, rancher, caretaker, biologist, researcher, scientist, health care provider. For example, the internal identifier may be utilized after a cow is killed and its meat is distributed to supermarkets if there is an outbreak of a disease related to that specific meat, such as E. coli or spongiform encephalopathy, so that a government agency can trace the meat all the way back to where it was born and lived and was killed. A biologist or researcher may also utilize this universal identifier to track migration patterns of organisms and a company that owns animals may utilize the animal's universal identifier to track the animal and claim ownership of a specific animal.

[00330] The number of panels or number of phenotypes or number of genetic variants, or number of genes or loci, or various combinations thereof, may be used to determine the level of service or price for determining an organism's risk or predisposition to or carrier status of various genetic variants or phenotypes or both. If a single panel is chosen, the sample for an organism that supplies the genetic material (such as buccal tissue, epithelial tissue, saliva, blood, hair, hair follicle, skin, etc.) may be used to test only that panel, or it may be used on a number of panels, but the results from only that panel is reported to the organism. If a subset of a panel is used, the organism's sample may be tested for only the phenotypes, such as conditions, chosen by the organism, or their sample may be used for the entire panel or a number of panels, but only the results from the phenotypes, such as conditions, chosen by the organism are reported. Results from genetic variants, phenotypes, such as conditions, or panels not chosen by the organism initially may be released to the organism if the organism chooses so at a later date. The organism's owner, or representative, or third party may have to pay an

additional cost. The organism may or may not submit another biologic sample. The conditions selected can be selected not only by the organism who's risk or predisposition or carrier status is being tested for, but can also be selected by another party, such as a parent, guardian, relative, health care manager, medical professional, or third party with the authority to, or may be selected by the organism with consultation of the aforementioned parties, or selected by the aforementioned parties with the consultation of the organism being tested.

[00331] Different levels of service with varying costs can also be provided where the initial analysis is followed with a consultation with a specialist. An organism's owner, or representative, or third party can choose a lower level of testing, for example, a single phenotype, such as a disease or condition, or a single genetic variant or single gene, and afterwards, decide to obtain a more comprehensive genetic profile or a full genetic profile. An organism's owner, or representative, or third party may choose to have an initial consultation with a veterinarian or specialist, and decide to have a consultation with a specialist referred to by the managing doctor or genetic counselor or physician assistant or nurse practitioner or other healthcare professional. In some cases, non-medical specialists may be consulted as well, either in conjunction with a medical specialist or independently.

[00332] After an organism's owner, or representative, or third party selects a genetic profile or genetic testing level, such as number of panels, choice of panel(s), number of genetic variants, number of genes or loci, number of phenotypes, such as conditions, and/or reflex testing, and/or the degree or depth or level of reflex testing, and/or OP-CADI, the organism may sign a waiver or other release or disclaimer and a biological sample is obtained from the organism for genetic testing. The sample may be linked to a number, such as a "Confidential Client Number" or CCN, which is given to the organism or the organism's healthcare provider or the person who ordered the test or other third party with authority to order the test or have access to the CCN. The organism's name and CCN can be encrypted and a single or multiple physical (non-electronic) copy or copies or electronic copy or copies of the information linking the organism's name to the CCN can be kept to maintain confidentiality.

[00333] Genetic samples can be obtained from kits provided to organisms with sample collection containers for the organism's biological sample. The kit may also provide instructions for an organism to directly collect their own sample, such as how much hair, urine, sweat, buccal tissue, tongue cells, or saliva to provide. The kit may also contain instructions for an organism to request tissue samples to be taken by a health care specialist, or instructions for how they can obtain their own biologic sample (as discussed above), to be stored indefinitely for the purpose of DNA banking (long-term storage of DNA for future use, such as analysis, or to pass on to future generations). The kit may also provide return packaging for the sample to be sent to a sample processing facility, where the organism's genetic material is then isolated from the biological sample for either storage or for genetic testing or both.

[00334] A genetic sample of DNA or RNA may be isolated from a biological sample according to any of several well-known biochemical and molecular biological methods, see, e.g., Sambrook, et al., *Molecular Cloning: A Laboratory Manual* (Cold Spring Harbor Laboratory, New York) (1989). There are also several commercially available kits and reagents for isolating DNA or RNA from biological samples, such as those available from DNA Genotek, Gentra Systems, Qiagen, Ambion, and other suppliers. Buccal sample kits are readily available commercially, such as the MasterAmp™ Buccal Swab DNA extraction kit from Epicentre Biotechnologies, as are kits for DNA extraction from blood samples such as Extract-N-Amp™ from Sigma Aldrich. DNA from other tissues may be obtained by digesting the tissue with proteases and heat, centrifuging the sample, and using phenol-chloroform to extract the unwanted materials, leaving the DNA in the aqueous phase. The DNA may then be further isolated by ethanol precipitation.

[00335] DNA may be collected using DNA self collection kit technology available, such as from DNA Genotek, an organism collects a specimen of saliva for clinical processing. The sample conveniently may be stored and shipped at room temperature. After delivery of the sample to an appropriate laboratory for processing, DNA is isolated by heat denaturing and protease digesting the sample, typically using reagents supplied by the collection kit supplier at 50°C for at least one hour. The sample is next centrifuged, and the supernatant is ethanol precipitated. The DNA pellet is suspended in a buffer appropriate for subsequent analysis. In some embodiments, the sample is obtained from a cheek swab.

[00336] A DNA sample may also be provided to the organism in a form visible to the human eye. This visible DNA can be placed in a sealed container, tube, vial, locket, charm, watch, necklace, mantle-piece, show-piece or other display casing that may or may not be part of the genetic report or given to the organism at the same time as the genetic report or both. The visible DNA may also be combined with a coloring or fluorescent agent in order to make it more visible against its background. This service may be at an additional cost. The DNA may be made visible either using a laboratory kit, such as EPICENTRE® Biotechnologies' MasterPure™ Complete DNA and RNA Purification Kit, Axygen Biosciences' AxyPrep™ Multisource Genomic DNA Miniprep Kit, Whatman's GenSpin™ Genomic DNA Purification Kit, or any other commercially available kits, or by using methods known in the arts, such as by the following methodology: placing saliva or buccal tissue into 3-5 milliliters of water in a container (saliva can be obtained by swishing the 3-5ml of water around in the mouth and then spitting into a container), add approximately 1-2 teaspoons of salt, then add in 1-2 milliliters of household dish soap, stir for approximately five minutes, then add 4-5 milliliters of denatured alcohol and wait 10-20 minutes. An organism may be interested in displaying their DNA. This visible DNA can be shipped back to the organism directly or handed to them in person, either by their physician, healthcare provider, genetic counselor, nurse practitioner, physician assistant, or other person who ordered the test, either along with their genetic report or at a separate time. This visible

DNA may be ordered along with genetic analysis or on its own. This service may incur an additional fee.

[00337] DNA art may also be provided to the organism in the form of pictures or drawings that show either part of their genetic code or their entire genetic code. The picture may be in the form of a black and white or color picture, photograph, image, or print out (such as of the data) of the array, microarray, massarray, beadarray, genechip, or sequencing (such as, for example, by utilizing shotgun sequencing, double-barrel shotgun sequencing, pyrosequencing, nanopores, fluorophores, or nanoballs) results from genetic testing that was conducted for that organism or for the organism's family, such as based on the panel they ordered, or may be a depiction or representation of part or the whole genome, such as their entire genetic code or a part of their genetic code, such as if sequencing or full genome sequencing is utilized. The pictures, photographs, video images, computer images, drawings, sketches, or any other images depicting an organism's or a family's genetic code, such as for a single genetic variant, multiple genetic variants, single gene, multiple genes, single locus, multiple loci, single chromosome, multiple chromosomes, partial genome, or full genome (such as sequence data, restriction fragment length polymorphisms, gel electrophoresis products, etc.) may be digital, printed, screened, via decalomania, via holography, drawn, painted, woven, such as into rugs, carpets or tapestries, and blown, such as with glassblowing, and may range in size from very small, such as wallet-size, such as one inch by one inch, to extremely large, such as billboard size or building wall size, such as 100 feet by 100 feet. DNA may be produced by the company that conducts the genetic testing or the genetic analysis, the laboratory (158) that processes the genetic sample and the genetic testing, or by another company, such as DNA 11 Inc. (Ottawa, Ontario, Canada). The DNA art may be produced from the same genetic sample that is used for genetic testing and/or analysis or it may be from a different genetic sample. The DNA art may appear within the genetic report, such as on the cover of the genetic report or within the genetic report, or be delivered with or around the same time as the genetic report, or at an earlier or later date, and may be ordered at the same time that the genetic testing, genetic analysis or genetic report is ordered or it may be ordered at a later time (utilizing either the same genetic material or new genetic material) or it may be ordered separately, on its own. This service may incur an additional fee.

[00338] RNA may also be used as the genetic sample. In particular, genetic variations that are expressed can be identified from mRNA. The term "messenger RNA" or "mRNA" includes, but is not limited to pre-mRNA transcript(s), transcript processing intermediates, mature mRNA(s) ready for translation and transcripts of the gene or genes, or nucleic acids derived from the mRNA transcript(s). Transcript processing may include splicing, editing and degradation. As used herein, a nucleic acid derived from an mRNA transcript refers to a nucleic acid for whose synthesis the mRNA transcript or a subsequence thereof has ultimately served as a template. Thus, a cDNA reverse transcribed from an mRNA, a DNA amplified from the cDNA, an RNA transcribed from the amplified DNA, etc., are all derived from the mRNA transcript. RNA may be isolated from any of several bodily tissues using

methods known in the art, such as isolation of RNA from unfractionated whole blood using the PAXgene™ Blood RNA System available from PreAnalytiX. Typically, mRNA may be used to reverse transcribe cDNA, which may then be used or amplified for gene variation analysis.

[00339] The methods described herein can be applied in the context of any platform capable of genotyping a sample, e.g., arrays, microarrays, massarrays, beadarrays, genechips, PCR-based techniques, exome sequencing, full (such as whole) exome sequencing, partial genome sequencing or full (such as whole) genome sequencing, such as with shotgun sequencing, double-barrel shotgun sequencing, pyrosequencing, nanopore sequencing (nanopores), fluorophore sequencing (fluorophores), DNA nanoball sequencing (nanoballs), or any other partial or full (such as whole) genome sequencing technologies. The terms "sequencing apparatus" and "sequencing platform" include but are not limited to arrays, nanopores, nanoballs, pyrosequencing, shotgun sequencing, double-barrel shotgun sequencing, SMRT™ Sequencing Technology or any other method of genetic sequencing that identifies the allele or genotype of one or more genetic variants in a genome. Often, results or data from a sequencing apparatus or a sequencing platform are provided as part of sequencing services. Prior to identifying a genetic variant, such as a polymorphism, through testing or analysis or both, a genetic sample is typically amplified, either from DNA or cDNA reverse transcribed from RNA, although other genetic testing methodologies may exist that may not require DNA amplification. DNA may be amplified by a number of methods, many of which employ PCR. See, for example, PCR Technology: Principles and Applications for DNA Amplification (Ed. H. A. Erlich, Freeman Press, NY, N.Y., 1992); PCR Protocols: A Guide to Methods and Applications (Eds. Innis, et al., Academic Press, San Diego, Calif., 1990); *Mattila et al., Nucleic Acids Res.* 19, 4967 (1991); *Eckert et al., PCR Methods and Applications* 1, 17 (1991); PCR (Eds. McPherson et al., IRL Press, Oxford); and U.S. Pat. Nos. 4,683,202, 4,683,195, 4,800,159 4,965,188, and 5,333,675, and each of which is incorporated herein by reference in their entireties for all purposes.

[00340] Other suitable amplification methods include the ligase chain reaction (LCR) (for example, *Wu and Wallace, Genomics* 4, 560 (1989), *Landegren et al., Science* 241, 1077 (1988) and *Barringer et al. Gene* 89:117 (1990)), transcription amplification (*Kwoh et al., Proc. Natl. Acad. Sci. USA* 86:1173-1177 (1989) and WO88/10315), self-sustained sequence replication (*Guatelli et al., Proc. Nat. Acad. Sci. USA*, 87:1874-1878 (1990) and WO90/06995), selective amplification of target polynucleotide sequences (U.S. Pat. No. 6,410,276), consensus sequence primed polymerase chain reaction (CP-PCR) (U.S. Pat. No. 4,437,975), arbitrarily primed polymerase chain reaction (AP-PCR) (U.S. Pat. Nos. 5,413,909, 5,861,245) nucleic acid based sequence amplification (NABSA), rolling circle amplification (RCA), multiple displacement amplification (MDA) (U.S. Pat. Nos. 6,124,120 and 6,323,009) and circle-to-circle amplification (C2CA) (*Dahl et al. Proc. Natl. Acad. Sci* 101:4548-4553 (2004)). (See, U.S. Pat. Nos. 5,409,818, 5,554,517, and 6,063,603, each of which is incorporated herein by reference). Other amplification methods that may be used are described in, U.S. Pat. Nos.

5,242,794, 5,494,810, 5,409,818, 4,988,617, 6,063,603 and 5,554,517 and in U.S. Ser. No. 09/854,317, each of which is incorporated herein by reference.

[00341] Several methods are known in the art to identify genetic variations and include, but are not limited to, DNA genotyping or sequencing or both by any of several methodologies, such as arrays, microarrays, genechips, bead arrays, massarrays, PCR based methods, nanopores, nanoballs, fluorophores, pyrosequencing, shotgun sequencing, double-barrel shotgun sequencing, sequencing by ligation, sequencing by synthesis, fragment length polymorphism assays (restriction fragment length polymorphism (RFLP), cleavage fragment length polymorphism (CFLP), cleaved amplified polymorphism (CAP)), hybridization methods using an allele-specific oligonucleotide as a template (e.g., TaqMan PCR method, the invader method, the DNA chip method), methods using a primer extension reaction, mass spectrometry (MALDI-TOF/MS method), fluorescence in situ hybridization, karyotyping, and the like.

[00342] A low density or mid density or high density DNA array, such as a microarray or massarray or bead array or genechip, can be used for genetic variant, such as SNP, identification, to generate a genotype(s) for one or more genetic variants (genetic testing that leads to a raw genotype profile for an organism) and profile generation. Such arrays or microarrays or bead arrays are commercially available, for example, from Affymetrix and Illumina (see Affymetrix GeneChip® 500K Assay Manual, Affymetrix, Santa Clara, CA (incorporated by reference); Sentrix® humanHap650Y genotyping beadchip, Illumina, San Diego, CA). In these assays, a subset of the human genome can be amplified through a single primer amplification reaction using restriction enzyme digested, adaptor-ligated human genomic DNA. The sample is denatured, labeled, and then hybridized to a microarray with small DNA probes at specific locations on a coated quartz surface. The amount of label that hybridizes to each probe as a function of the amplified DNA sequence is monitored, thereby yielding sequence information and resultant SNP identification. For example, use of the Affymetrix GeneChip 500K Assay is carried out according to the manufacturer's directions. Briefly, isolated genomic DNA is first digested with either a NspI or StyI restriction endonuclease. The digested DNA is then ligated with a NspI or StyI adaptor oligonucleotide that respectively anneals to either the NspI or StyI restricted DNA. The adaptor-containing DNA following ligation is then amplified by PCR to yield amplified DNA fragments between about 200 and 1100 base pairs, as confirmed by gel electrophoresis. PCR products that meet the amplification standard are purified and quantified for fragmentation. The PCR products are fragmented with DNase I for optimal DNA chip hybridization. Following fragmentation, DNA fragments should be less than 250 base pairs, and on average, about 180 base pairs, as confirmed by gel electrophoresis. Samples that meet the fragmentation standard are then labeled with a biotin compound using terminal deoxynucleotidyl transferase. The labeled fragments are next denatured and then hybridized into a GeneChip 250K array. Following hybridization, the array is stained prior to scanning in a three step process consisting of a streptavidin phycoerythrin (SAPE) stain, followed by an antibody amplification step with a biotinylated, anti-

streptavidin antibody (goat), and final stain with streptavidin phycoerythrin (SAPE). After labeling, the array is covered with an array holding buffer and then scanned with a scanner such as the Affymetrix GeneChip Scanner 3000. Analysis of data following scanning of an Affymetrix GeneChip Human Mapping 500K Array Set is performed according to the manufacturer's guidelines.

[00343] As an alternative to, or in addition to, DNA array, microarray, massarray, or bead array analysis, genetic variations such as SNPs, DIPs and mutations can be detected by DNA sequencing. DNA sequencing may also be used to sequence a small portion (such as one full gene or a portion of one gene), a substantial portion (such as multiple genes or multiple chromosomes), or the entire genomic sequence of an organism. Traditionally, common DNA sequencing has been based the technique known as Sanger sequencing which uses polyacrylamide gel fractionation to resolve a population of chain-terminated fragments (*Sanger et al., Proc. Natl. Acad. Sci. USA 74:5463-5467 (1977)*). Alternative methods have been and continue to be developed to increase the speed and ease of DNA sequencing. For example, high throughput and single molecule sequencing platforms are commercially available or under development from 454 Life Sciences (Branford, CT) (*Margulies et al., Nature (2005) 437:376-380 (2005)*); Solexa (Hayward, CA), acquired by Illumina, Inc. (San Diego, CA); Helicos BioSciences Corporation (Cambridge, MA) (U.S. application Ser. No. 11/167046, filed June 23, 2005), and Li-Cor Biosciences (Lincoln, NE) (U.S. application Ser. No. 11/118031, filed April 29, 2005). Shotgun sequencing and double-barrel shotgun sequencing are also sequencing methods. Nanopore sequencing (nanopores) is one such method that may allow for high throughput DNA sequencing (Vercoutere, W. et al. *Nature Biotechnology* 19, 248-252 (2001), Sauer-Budge, A.F. et al. *Phys. Rev. Lett.* 90, 238101-238101 - 238101-238104 (2003), Howorka, S. *Nat Biotechnol.* 2001 Jul;19(7):636-9). Nanopores may be used to sequence a small portion (such as one full gene or a portion of one gene), a substantial portion (such as multiple genes or multiple chromosomes), or the entire genomic sequence of an organism. Nanopore sequencing technology may be commercially available or under development from Sequenom (San Diego, CA), Illumina (San Diego, CA), Oxford Nanopore Technologies LTD (Kidlington, United Kingdom), and Agilent Laboratories (Santa Clara, CA). Nanopore sequencing methods and apparatus are have been described in the art and for example are provided in US Patent No. 5,795,782, herein incorporated by reference in its entirety. Other sequencing technologies include nanoballs, fluorophores and Single Molecule Real Time DNA sequencing technology (SMRT™) technology, and pyrosequencing, as described in US Patent Nos. 7,371,851; 7,405,281; 7,170,050; 7,244,567; 7,244,559; 7,264,929; 7,323,305; 7,211,390; and 7,335,762; and in US Patent Application Publication Nos. US2009/0053724; US2007/0231804; US2009/0024331; US2008/0206764; US2009/0011943; US2009/0005252; and US2008/0171331; US2008/0213771 herein incorporated by reference in their entirety.

[00344] For example, a low-, medium- or high-density array, such as the commercially available platforms from Sequenom or Affymetrix or Illumina, is used for genetic variant identification and

profile generation. As technology evolves, there may be other technology vendors who can generate low-, medium- or high-density genotype (such as genetic variant or polymorphism or mutation or copy number variation) profiles. The massarray or microarray or beadarray can have at least 1000, 5000, 6,000, 6,500, 7,000, 8,000, 10,000, 15,000, 20,000, 25,000, 30,000, 45,000, or 50,000 unique oligonucleotide sequences. Each oligonucleotide sequence may exist one or more times on the array, such as for redundancy or to increase accuracy, as the same (non-unique) oligonucleotide sequence may test for the same genetic variant and therefore these oligonucleotide sequences (which test for the same exact genetic variant) are not unique; only oligonucleotide sequences that test for or detect different genetic variants are considered herein unique oligonucleotide sequences. A genetic variant may be unique if it exists in a different location within the genome, even if it is just one basepair away from another genetic variant, or it may also be unique if it occurs at the same exact location within the genome but encompasses a different type of variation, such as a different nucleotide change. For example, if two genetic variants occur at the same exact location but one is the change from an Adenine (A) to a Guanine (G) and the other is a change from an Adenine (A) to a Thymine (T), then this constitutes a unique genetic variant and two unique probes, such as oligonucleotide sequences, may be needed to detect these changes (one unique oligonucleotide sequence to test for or detect the A to G change and the other unique oligonucleotide sequence to test for or detect the A to T change). Each of the unique oligonucleotide sequences corresponds to, or is associated with, a genetic variant, such as a genetic polymorphism, such as a SNP. For example, each sequence may be associated with a phenotype that is medically relevant or linked to at least one phenotype as reported in published literature. For example, an oligonucleotide sequence can comprise a genetic variant, be a sequence in linkage disequilibrium with a genetic variant, such as a SNP, or contain genetic sequence immediately flanking the genetic variant of about 5, 10, 15, 20, 25, 30, 35, 40, 45, 50, 60, 75, 100, or more bps upstream or downstream of a genetic variant. The genetic variant may be medically related or non-medically related. The genetic variant may be trait related or non-trait related. In other embodiments, each of the unique oligonucleotide sequences on an array is associated with a genetic variant, such as a polymorphism or mutation that is medically relevant or provides information about a trait, for example, each sequence on the array is associated with a SNP that is correlated with a disease or condition or trait. For example, the sequences on the array may be used to detect the genetic variants in the non-limiting examples of representative genes listed in **Table 4**. Other non-limiting examples of representative genes may include those listed in **FIGS. 15-20**. The array may comprise sequences that detect a genetic variation, such as a SNP, in each of the non-limiting examples of representative genes listed in **Table 4**, or those listed in **FIG. 15-20**, that is associated with a genetic condition or phenotype. Some arrays may have oligonucleotide sequences, wherein at least 50, 70, 75, 80, 85, 90, or 95% of the sequences are associated with a genetic variant that is medically relevant. In some embodiments, at least 5, 10, 15, 20, 25, 30, 50, 75, 100, 125, 150, 175, 200, 250, 300, 400, 500, 1000 or more unique phenotypes are associated with the genetic variants on the array. In some

embodiments, each of the oligonucleotides on the array is associated with a different genetic variant or a different phenotype, such as a disease or condition. In some arrays, different oligonucleotides may be associated with the same phenotype, such as a disease or condition.

[00345] Arrays can also have oligonucleotide sequences wherein at least 5, 10, 25, 50, 65, 70, or 75% of the sequences corresponding to a genetic variant, such as SNP, are unique sequences or sequences not listed in a public database, for example sequences immediately flanking the genetic variant that are about 5, 10, 20, 25, 30, 35, 40, 45, 50, 60, 75, 100, 200, or more bps upstream or downstream of a genetic variant. The oligonucleotides on an array may detect at least about 10, 20, 50, 75, 100, 1000, 5000, 6,000, 6,500, 7,000, 8,000, 10,000, 15,000, 20,000, 25,000, 30,000, 45,000, 50,000, 100,000, 150,000, 200,000, 250,000, 300,000, 350,000, 400,000, 450,000, 500,000, 750,000, 1,000,000, 1,500,000, 2,000,000, 2,500,000, 3,000,000, 3,500,000, 4,000,000, 4,500,000, 5,000,000, 5,500,000, 6,000,000, 6,500,000, 7,000,000, 7,500,000, 8,000,000, 8,500,000, 9,000,000, 9,500,000, 10,000,000 or more genetic variants, such as SNPs. The number of genetic variants may be present in at least approximately 2, 5, 10, 15, 20, 100, 250, 500, 750, 1000, 1250, 1500, 2000, 3000, 3500, 4000, 4500, 5000, 5500, 6000, 6500, 7000, 7500, 8000, 8500, 9000, 9500, 10,000, 10,500, 11000, 11500, 12000, 12500, 13,000, 13,500, 14,000, 14,500, 15,000, 15,500, 16,000, 16,500, 17,000, 17,500, 18,000, 18500, 19000, 19500, or 20,000 genes. In some embodiments, each sequence on an array is used to determine or calculate an organ system score. In other embodiments, each of the sequences is used to determine or calculate at least 2 or more organ system scores. Some arrays contain sequences wherein each of the sequences is used to determine or calculate a score for a medical specialty. In yet other embodiments, each of the sequences are used to calculate or obtain an overall genetic health score. In some embodiments, the array comprises unique oligonucleotide sequences that detect at least 2, 5, 10, 50, 100, 200, 500, 1,000, 2,000, 5000 medically-relevant genetic variants or SNPs, at least 6000 medically-relevant genetic variants or SNPs, or at least 6500 medically-relevant genetic variants or SNPs. Medically-relevant genetic variants or SNPs refer to a genetic variant that has been associated or linked in published literature, such as a published journal article, with either an increased or decreased risk or predisposition to disease or medical condition or associated with being a carrier or affected or likely-affected by a disease or medical condition. The number of unique medically relevant phenotypes associated with genetic variants that the unique oligonucleotides may be able to test for or detect may include at least 25, 50, 75, 100, 150, 200, 250, 300, 350, 400, 450, 500, 550, 600 or more phenotypes.

[00346] The genetic variants detected by the array may be present in non-coding regions. The genetic variants may be medically related or non-medically related. The genetic variants may include only clinically relevant genetic variants, or genetic variants in genes or in linkage disequilibrium of other genetic variants, correlated with clinical phenotypes, such as diseases or medical conditions. The genetic variants may be organized by medical specialty, gene, location on a chromosome, phenotype or disease. The genetic variants may be organized by trait or with similar groups of traits. The genetic

variants can be organized by clinical severity or by how well that genetic variant is thought to correlate with a specific phenotype, such as a disease or condition. The private database can also have precise information for each genetic variant. For example, information such as odds ratio or other risk value, applicable species/genus or populations, inheritance patterns, journal references, journal links, brief genetic variant synopsis, phenotype-associated allele or genotype, p-value of the association, confidence interval of the risk value, incidence or prevalence of the phenotype, frequencies of the alleles or genotypes, or both, of the genetic variant, different scoring systems for the genetic variant-phenotype association (as previously discussed), such as the GVP score, and recommendations.

[00347] In some embodiments, each of the genetic variants detected by the array is medically relevant. In some embodiments, each of the sequences on the array is linked to a journal reference or a recommendation, directly or indirectly (for example, if the sequence is linked to a condition, wherein the condition is linked to a journal reference or recommendation or both). In other embodiments, each of the sequences on the array is for a specific phenotype, such as a disease, or for a specific genetic testing, such as for children, for carrier information, or for cancer patients. The array can have sequences wherein each sequence, or a subset of the sequences, is used to determine the pharmacogenomic profile of an organism.

[00348] For example, each sequence on an array, or a subset of sequences on the array may be used to determine the risk of phenotypes, such as conditions, or carrier status or both in the panels. A single array may represent multiple panels (2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15 or more) or may represent a single panel. The option is also available to choose different demoninations, such as a Custom 10 Panel, which tests for 10 phenotypes or a Custom 20 Panel, which tests for 20 phenotypes. Custom panels can range from one phenotype to over 1,000 phenotypes. The Custom Panel may have approximately, 5, 10, 15, 20, 25, 30, 40, 50, 60, 75, 100, 150, 200, 250, 300, 400, 500, 1000 or more phenotypes, such as diseases or traits.

[00349] A single array (meaing any type of genetic testing array, such as microarray, massarray, genechip or beadarray) may comprise sequences used to determine the degree of risk of phenotypes, such as diseases or traits, or carrier status, or both, on a number of panels, or all of the panels. Alternatively, the degree of risk or predisposition to the phenotypes, such as diseases or traits, or carrier status, or both on one or more panels can be determined using any platform capable of genotyping a sample, e.g., microarrays, massarrays, bead arrays, PCR-based techniques, exome sequencing, or genome sequencing including partial or full genome sequencing, such as nanopore sequencing (herein refered to as nanopores).

[00350] Each panel can be used to detect all the phenotypes listed for each panel or a subset of the phenotypes listed.

[00351] As illustrated in **FIG. 1**, the results **(120)**, obtained from the genetic sample, for example, obtained by microarray analysis or sequencing analysis, can be sent to the central location **(104)**, and analysis of the isolated genetic sample and generation of a raw (unanalyzed in terms of associations

with phenotypes) genetic genotype profile is performed. The results and statistical analysis (such as p-values, accuracy, reproducibility, reliability or any other relevant values for each of the genetic variants detected) can be transmitted at step (122), (124), or (126) to a location, for example, where an organism submitted their sample. The raw genotype results and statistical analysis may then be stored, partially analyzed or fully analyzed in order to generate a genetic report (report) to present to the organism (as described further below). The report, results and analysis can be transmitted securely over a network. Alternatively, the report may not be transmitted at all over a network, but is printed in hard copy and stored in hard copy only such that no electronic version is stored. Alternatively, an electronic version is stored, but only with an identification number (such as the CCN). Three different types of reports may be generated, one for a GC, one for the physician or the person or entity that ordered the genetic profile, and one for the organism, wherein each report is tailored to each person reading the report (who that specific report was sent or given to), respectively.

[00352] FIG. 11A is a block diagram showing a representative example logic device through which results can be received and analyzed to generate a report. FIG. 11A shows a computer system (or digital device) 800 to receive and store results, analyze the results, and produce a report of the results and analysis. The computer system 800 may be understood as a logical apparatus that can read instructions from media 811 and/or network port 805, which can optionally be connected to server 809 having fixed media 812. The system shown in FIG. 11A includes CPU 801, disk drives 803, optional input devices such as keyboard 815 and/or mouse 816 and optional monitor 807. (Parts 800, 801, 803, 805, 807, 811, 815 and 816 are also depicted in FIG. 11B). Data communication can be achieved through the indicated communication medium to a server 809 at a local or a remote location. The communication medium can include any means of transmitting and/or receiving data. For example, the communication medium can be a network connection, a wireless connection or an internet connection. Such a connection can provide for communication over the World Wide Web. It is envisioned that data relating to the present invention can be transmitted over such networks or connections for reception and/or for review by a party 822. The receiving party 822 can be but is not limited to an organism, a health care provider or a health care manager. In one embodiment, a computer-readable medium includes a medium suitable for transmission of a result of an analysis of a biological sample. The medium can include a result regarding analysis of an organism's genetic profile, wherein such a result is derived using the methods described herein.

[00353] FIG. 11B is a schematic of a non-limiting example of the general steps for obtaining a genetic analysis of a sample obtained from an organism; the example includes a computer system that can be used for receiving, storing, and analyzing data from genotyping, genetic testing and/or genetic analysis.

[00354] In step 902 of FIG. 11B, a sample of genetic material 904 of an organism is obtained or isolated from a biological sample of an organism (e.g. blood, hair, skin, saliva, semen, buccal cells, epithelial tissue, and various bodily tissues). The genetic sample 904 may be obtained by a variety of

methods known in the art. In step 906 raw genetic data (e.g. genomic sequence, SNP profiles, etc.) are stored on the computer 800 (also described in FIG. 11A). All or a portion of the data may be input by a user interface such as a mouse 816(also described in FIG. 11A) or a keyboard 815 (also described in FIG. 11A). Alternatively, the computer may be connected to the genotyping or genome sequencing apparatus or platform via a network port 805 (also described in FIG. 11A), or the computer may be a part of the genotyping apparatus, or the data may be input by loading of removable media 811 (also described in FIG. 11A). The genetic data may be stored on removable media such as a removable disk 811 or non-removable media such as a hard disk drive or a solid state disk drive 803 (also described in FIG. 11A). The data and or results may be displayed at any time on a computer display 807(also described in FIG. 11A) such as a monitor and may also be stored or printed at any time in the form of a genetic report. In step 908, genetic variants associated with phenotypes are obtained from scientific literature and sent to a computer system 800. The alleles or genotypes of each genetic variation or polymorphism identified from the genetic sample are then reviewed to determine whether the presence or absence of a particular allele or genotype is associated with a phenotype of interest.

[00355] The genotype variants and results from the biological samples are sent to, stored, and analyzed by a computer system (or digital device) 800, which produces a report of the results and analyses of the genomic data. The results and analyses may be accessed online by subscribers or their health care managers via an online portal or website as in step 910. The results and analyses can be viewed online, saved on a subscriber's computer, printed, or have mailed to the subscriber or health care manager 912. The organism may obtain genetic counseling or present the reports to physicians and other health professionals for personalized health management 914.

[00356] Genetic data, such as raw genotype code or data during the analysis process, such as during the analysis of the raw genotype code and during its correlation with phenotypes, or analyzed data, such as that which may appear or does appear within the genetic report, may also be displayable through virtual reality (VR) technology. The user who is viewing the genetic data through VR may be able to manipulate and change the genetic data, the genetic analysis, or any of the analytical processes, while being within the VR environment, either through the use of keyboard, control pad, mouse, wand or other pointing device, input device, audio and/or phonetic device(s), eye sensor that tracks the movement of the user's eye(s), tactile glove(s), or tactile suit. The VR environment may be viewable on a computer screen, or through the use of goggles, eye lenses or other optics, a helmet or other headpiece, or a VR room or other enclosed space, such as a VR machine that is large enough for one or more organisms to enter, either partially or fully. A Predictive Medicine Database, or other database containing genomic information, may also be viewable and/or modifiable via VR, as described above. Methods and apparatus for manipulating data with VR technology in general are known in the art and are described for example in US Patent Application Publication No. 20030033150, herein incorporated by reference in its entirety.

[00357] The computer system can also have a database of oligonucleotides sequences as described herein. For example, the computer system can have a database with at least 2, 5, 10, 15, 20, 25, 50, 75, 100, 150, 200, 250, 500, 1000, 5000, 10000, 15000, 20000, 30000, 40000 or more oligonucleotide sequences and each of the sequences are associated with a genetic variant, such as a polymorphism. The database may have a variety of optional components that, for example, provide more information about the phenotypes. In some embodiments there is provided a computer readable medium encoded with computer executable software that includes instructions for a computer to execute functions associated with the identified genetic variants. Such computer system may include any combination of such codes or computer executable software, depending upon the types of evaluations desired to be completed. The computer system may also have code for linking each of the sequences to at least one phenotype, such as a condition, for example, a medical condition. Each medical condition in turn can be linked to at least one recommendation by a medical specialist and code for generating a report comprising the recommendation. The system can have code for calculating one or more scores for a phenotype, such as a condition or trait, for an organism, one or more action scores, one or more predictive medicine risk scores or carrier status or both, one or more organ system scores, or an overall genetic health score. The system can further comprise code for linking each of the sequences to at least one citation for a published journal article, such as a peer-reviewed journal article, showing the correlation between the genetic variation associated with the sequence to a phenotype, such as a condition or trait. The system can also have code for conducting genetic analysis based on specific panel(s) chosen. The system can also have code for one or more of the following: conducting, analyzing, organizing or reporting the results of reflex testing, as described herein. The system can also have code for generating a report. Different types of reports can be generated, for example, reports based on the level of detail an organism may want or have paid for. For example, an organism may have ordered analysis for a single phenotype, such as a condition, and thus a report may comprise the results for that single phenotype, such as a condition. Another organism may have requested a genetic profile for a panel or an organ system, or another organism may have requested a comprehensive genetic profile that includes analysis of all clinically relevant genetic variants with full reflex testing. The reports for each of the organisms can represent each of their requests.

[00358] The analysis generated can be reviewed and further analyzed by a veterinarian or researcher or persona trained in genetic analysis, or other health care specialist, or other third party, in "Post-test", for example as shown in **FIG. 1**. This person or group of people can meet with the organism's owners, or representative, or third party to discuss the results, analysis, and/or the genetic report (such as shown in **FIG. 12A-G**). Discussions can include information about the genetic variant(s), such as the genetic variant(s) (for example, polymorphism(s)) that is or are detected, how they can be inherited or transmitted (for example using the pedigree generated from the questionnaire), the prevalence of the genetic variant, prevalence or incidence of the phenotype, and information about the phenotype (for example, specific conditions or traits, such as medically or clinically relevant

conditions), such as how the phenotype may affect the organism, results of reflex testing (as described herein), and if adverse conditions, preventative measures are associated with the genetic variants identified and analyzed or the phenotype(s) identified and analyzed or both. The GC or medical professional may incorporate other information, such as other genetic information or information from questionnaires in their analysis and discussion with the organism. Information about the phenotype, such as condition or trait, can include recommendations, such as follow-up suggestions such as further genetic counseling (**FIG. 1**) or predictive medicine recommendations or preventive medicine recommendations for the organism's personal physician or other healthcare provider (**132**). Screening information, such as methods of breast cancer screening, may be discussed for example if an organism is found to be at a higher risk of breast cancer. Other topics that may be discussed include habit modifications and medications. For example, habit modifications may be suggested such as dietary changes and specific diet plans may be recommended or an exercise regimen may be suggested and specific exercise facilities or trainers may be referred to the organism. Common misconceptions may also be included, allowing the organism to be aware of preventive measures or other interventions that may be thought of as being helpful or useful but that have been shown in published literature to either not be beneficial or to actually be harmful. Alternative therapies may also be included, such as alternative medicines, such as fish oil supplements, or alternative therapies, such as acupuncture or yoga. Family planning options may also be included, as well as monitoring options, such as screening exams or laboratory tests that may detect or help monitor for the presence of a phenotype, or the progression of a phenotype. Medications that may prevent, limit the onset or delay the progression of a phenotype, such as a disease, the organism is predisposed to, or a medication with high efficacy and low side effects may be suggested for an organism, or medications or classes of medications that an organism should avoid due to possibility of adverse reaction(s). For example, the medical professional may make an assessment of the organism's likely drug response including metabolism, efficacy and/or safety. The medical professional can also discuss therapeutic treatments, such as prophylactic treatments and monitoring (such as doctor visits and exams, radiologic exams, or laboratory tests) for potential need of treatment or effects of treatment based on information from the organism's genetic profile either alone or in combination with information about the organism's non-genetic factors (such as , habits, diagnosed medical conditions, current medications, and others). Additional resources may also be listed, such as including information for the organism or the organism's physician or other healthcare professional to acquire additional information about the phenotype or the genetic variant(s) or both, such as links to websites that contain information on the phenotype, such as an internal website from the company that produces the genetic report or external websites, such as national organizations for the phenotype. Additional resources may also include reference to telephone numbers, books, or organisms that the organism may seek out to acquire more information about the phenotype or the genetic variant(s) or both.

[00359] A report with the results and analysis, can include information such as shown in **FIG. 6**, and be given to the organism during the consultation. Alternatively, the report, or a genetic report is depicted in **FIG. 12**. Reports may or may not typically also include a recommendation option by a physician or other licensed medical professional. In some embodiments, an organism may choose to further consult with a medical specialist or be referred to a medical specialist. Another report specific for the organism's physician (such as a 'Healthcare Professional Summary') can also be generated and given to the organism or the organism's physician such as depicted in **FIG. 12E**. The report can contain a patient summary, recommendations that may include follow-up recommendations, screening information, modifications, alternative therapies or interventions, common misconceptions, monitoring information, family planning information, references to additional resources, medications, organ system scores(s), overall genetic health score, and a clinician summary. The recommendation options may be linked to a phenotype, such as a disease or trait, and can be presented in the report.

[00360] For example, an organism may have a disease for which they have either an increased or decreased risk of based on their genetic profile, and that disease is linked to a specific recommendation which is presented within the report generated for the organism.

[00361] Reports may also contain other information, such as habits tailored to an organism, based on the organism's genetic profile, such as during the initial round of genetic testing or analysis or ascertained through reflex testing.

[00362] Thus, the report for an organism's genetic profile, or Genetic Report can contain information about an organism's genotypes or phenotypes or both, as well as information directly related to that genotype or phenotype concerning preventive medicine recommendation options or intervention options or both (for example, **FIG. 12A-G**). The analysis of the genotypic and phenotypic data can include linked analysis and inclusion in the Genetic Report of all pertinent preventive medicine recommendation options or intervention options or both. Because many phenotypes, such as common diseases, are multifactorial, adjusting certain key non-genetic factors (such as modifications) may help to decrease the risk and incidence of the phenotype, such as disease or condition, even in those organisms found to have a genetic predisposition for that phenotype, such as disease or condition (for example, **FIG. 24**). . The genetic analysis process and the Genetic Report may link a phenotype, such as disease, risk with preventive measure options.

[00363] In one aspect, Genetically Tailored Prevention (GTP) and/or Preventive Measures (PMs) based on Preventive Medicine Recommendations or Interventions (PMRI's) are included in the Genetic Reports. PMs based on PMRIs can be ascertained through a review of all current literature and both published and non-published studies concerning preventive measures that are shown to decrease the incidence or progression of the disease or both, or to delay time until disease onset (allow the organism to live longer without the disease or symptoms of the disease manifesting) or decrease the morbidity or mortality related to the disease, or both. Some of the PMs based on PMRI's may

also be linked to specific genetic variants that increase or decrease risk for a phenotype while others may be linked to the phenotype as a whole.

[00364] Two or more distinct Genetic Reports can be generated from the analysis of the same organism's genetic material. For example, one genetic report may be created for the patient and another genetic report may be created for the physician who ordered the test. Other targeted Genetic Reports may be created for other third parties, such as the Department of Agriculture or other governmental agency,

[00365] The generation of Genetic Reports, or the genetic profiles for generating them, may be subject to different levels of service, such as for the reflex testing for ordered panel(s) or phenotype(s) or both. For instance, a low-cost service may be available whereas no reflex testing is available for any of the panel or phenotypes or both, a medium-cost service may be available where reflex testing goes only to round 2 and no further, and a high-cost service may be available where reflex testing goes through as many rounds as needed until no further reflex testing rounds exist. The panels themselves may also be differentiated by price, with certain panels that analyze a greater number of genetic variants or phenotypes, for both, incurring an additional or higher fee compared with other panels that analyze a lesser number of phenotypes. OP-CADI also may be a different level of service that may have an additional or different fee associated with it.

[00366] In some embodiments, the level of service may be changed or altered at any time, and may incur an additional fee. For example, an organism may originally have selected the low-cost service but after reviewing their Genetic Report, they order another analysis to be conducted and Genetic Report to be compiled utilizing the same exact genotype data, or by supplying new genetic material for genetic testing and new genotyping, but this time with a high-level of service that gives results about all possible reflex testing relating to the panel or phenotypes they ordered, or both.

[00367] An organism's owner, or representative, or third party with a pending genetic profile or genetic report to be generated for an organism may choose at any later date to have one or more of the following added to their analysis: reflex testing, additional panels, phenotypes, genes, specific genetic variant(s), or updated analysis based on updated or more recent research and genetic variant-phenotype association data. This additional genetic analysis and Genetic Report generation may require an additional fee. This additional analysis and report generation may be accomplished by utilizing the organism's raw genotype data from the original analysis or by ascertaining new genotype data by running either a stored biologic specimen (such as saliva, blood, tissue, hair, buccal tissue, such as from a buccal swab, purified DNA, etc.) or a new biologic specimen from the same organism through the genetic testing process at the laboratory.

[00368] The following examples illustrate and explain the present invention. The scope of the present invention is not limited by these examples. It should be noted that although the following examples are directed to use of the subject methods in human, similar methods can be applied to all non-human living subjects.

EXAMPLES

Example 1 (prophetic example): Genetic Profile for a Human Male Individual

[00369] A healthy male organism fills out a short, five minute 'Presymptomatic Genetic Testing Questionnaire' in person. The questionnaire includes questions on his current medical history, his family history including any known diseases, and any medications he is currently taking. There are also questions concerning his daily habits (such as tobacco, alcohol, caffeine, and drug use) along with his current exercise regimen. The completed questionnaire is reviewed by the presymptomatic genetic counselor (GC) who also may construct a genetic pedigree based on the male organism's (proband's) family history (**FIG. 2**). The GC briefly reviews his past medical and family history and gives the organism a copy of his genetic pedigree analysis that has already been conducted on his behalf. The GC tells the organism more in-depth information regarding further genetic testing services, different genetic testing options and panels available and, based on the organism's background, the GC recommends the Platinum Executive Package, also known as the Executive Panel Alpha, which analyzes thousands of genes and possible disease predispositions. The proband and the GC also briefly discuss the different cut-off and threshold values to be used during his genetic analysis, and the proband decides that he wants to be told about genetic variant-phenotype associations that may not be fully replicated yet, so the GVP score cut-off is set at greater than or equal to 0.75. The organism agrees on the Platinum Executive Package and signs a legal waiver. The GC takes a cheek swab sample and gives the organism a Confidential Client Number (CCN). He is shown that this corresponds to the client number printed on his cheek swab samples. The GC explains that his genetic data is never linked with his name or any other identifiable information except for his Confidential Client Number (CCN), in order to ensure the highest level of confidentiality. The GC gives the client's name and the corresponding CCN to the Managing Doctor who keeps a single copy of this encrypted information linking the CCN with the client's name in a fire-safe vault that is not kept online.

[00370] A follow-up appointment is scheduled with the same presymptomatic GC. The sample is sent to the lab by overnight courier and after the processing time to conduct the genetic material purification and genetic testing, the lab electronically transmits back to the central location and the results and recommendations based on the client's complete genetic profile are generated. The recommendations are included in an enhanced report, also known as the genetic report, is printed out and reviewed by the organism's GC. A managing doctor may also review and sign the report and may also discuss the results with the GC. The report includes information on the relevant genetic variants and their phenotypes that have been detected, including: ADORA2A, KALRN, 8q24, VKORC1, IRF5, and LRP6.

[00371] 1) Polymorphism in ADORA2A gene detected. This specific polymorphism has been shown to greatly increase a person's sensitivity to caffeine. Increased caffeine sensitivity has been

shown (specifically for this polymorphism) to correlate with reduced sleep quality and an increased risk of insomnia. Because of this, the following recommendations are made:

[00372] Organism has a genetic change that makes his body more sensitive to caffeine and that caffeine intake, even in the morning, may be affecting his sleep quality at night. Because of this, the organism may be advised to decrease or completely avoid products containing caffeine. He may also be advised that caffeine can be a difficult substance to stop using but that if he decreases his intake over a few weeks, he should be able to wean himself off it completely. Doing so may actually make him feel more awake and alert in the long run, since his sleep quality should improve. Based on the reflex testing conducting, he is also found to not be genetically predisposed to habitual caffeine use.

[00373] 2) Polymorphism in KALRN gene detected. This specific polymorphism is thought to account for over 12% of all early-onset coronary artery disease for Caucasians. Because of this, the following recommendations are made:

[00374] Organism has more than a 100 times greater likelihood of having early-onset coronary artery disease than the general population's risk of early-onset coronary artery disease. Due to this increased risk, the organism may consider instituting numerous modifications. His diet may be modified to limit his intake of trans-fats (such as hydrogenated oils that exist in fried foods, cakes, cookies, and margarine). The organism may also increase his exercise regimen, for example one option is that he exercises at least three times/week for at least 20 minutes per session.

[00375] The increased likelihood of early onset coronary artery disease also should be discussed with organism's primary care physician. Increased surveillance may help monitor disease onset and progression, such as yearly cholesterol blood tests. The organism is advised to discuss with his physician other possible methods to screen for plaque build-up in his coronary arteries, such as Echocardiograms and/or Nuclear Medicine Stress Testing (such as Adenosine-Thallium Scans).

[00376] The organism is also advised to discuss with his primary care physician the benefits and disadvantages of once a day low dose Aspirin therapy. Aspirin therapy may help decrease the risk of heart attacks and in the organism's future. (If the organism is interested in making an appointment with a local Cardiologist, the GC or report may provide him with a referral or list of cardiologists in his community.)

[00377] 3) Polymorphism in locus 8q24 detected. This polymorphism is associated with an increased risk for prostate cancer.

[00378] Due to organism's family history of prostate cancer along with a genetic polymorphism that is strongly associated with prostate cancer, the organism may be genetically predisposed to prostate cancer. This result should be discussed with his primary care physician. The importance of yearly screening exams for prostate cancer are made clear to the organism and he is instructed that he should always make sure to go for his annual exam and to make sure his prostate is always checked for possible warning signs of cancer or precancer. With proper screening, the impact of prostate cancer may be limited in his future, if it should develop.

[00379] Alternatively, the organism may also want to discuss this finding with an Urologist, who may advise for more radical screening modalities, such as yearly blood tests and possible radiological imaging of the prostate.

[00380] The organism is advised that now that he is aware of this predisposition, he can be empowered over it by making sure to stay connected with a healthcare professional that may screen him regularly for this disease so that they can take prompt action if it should ever manifest.

[00381] 4) Polymorphism in VKORC1 detected (homozygous). This specific polymorphism has been shown to be associated with sensitivity for a frequently used blood-thinning medication called warfarin (Coumadin).

[00382] Warfarin is an oral medication frequently used in order to thin a person's blood to either avoid or treat a history of blood clots. The organism is advised that it is very important to discuss this with his primary care physician and that he should also consider adding this information to his official medical record. If he is given warfarin at the usual dosage, then he is at a much greater risk of bleeding complications. As long as this issue is known, however, then physicians may be able to take steps to avoid any potentially harmful effects of this medication if prescribing it to the proband ever becomes necessary. For example, his physician may start the medication at a lower dose and titrate up carefully, making sure to monitor him closely to make sure his blood does not become too thin. Recent studies have also shown that concomitant application of low dose vitamin K may also significantly reduce intra-organism warfarin dose variation and the organism's physician should also consider this as an option if the proband is ever required to take Coumadin.

[00383] 5) Multiple polymorphisms in IRF5 detected. This specific group of polymorphisms has been shown to confer protection against Systemic Lupus Erythematosus (Lupus).

[00384] The organism is told about Lupus and that changes to his genetic code actually have been shown to protect him against Lupus. Because of this, he is 24% less likely to get Lupus than the general population's risk for Lupus.

[00385] 6) Polymorphisms in LRP6 found along with no APOE4 polymorphisms detected. These genetic polymorphisms, along with absence of APOE4, have been shown to protect against Alzheimer Disease.

[00386] The organism is told that due to changes in one of his genes, he is actually protected against Alzheimer Disease. His likelihood of getting Alzheimer Disease is considerably lower than that of the general population.

[00387] The GC and the organism finish reviewing the rest of the findings. The organism's GC and the managing physician then review these six findings discussed above, along with the other findings, with the organism and discuss some of the many genes that he did not have any polymorphisms in. The organism is advised that his family members may also benefit from genetic testing because they may contain the same polymorphisms that were detected in the organism or they may contain different genetic variants or different combinations of variants that may put them at risk for different diseases.

[00388] These recommendations are handed to the organism in a confidential envelope as an Enhanced Client Report, also known as a Genetic Report, and an Enhanced Physician's Report, also known as the Healthcare Professional Summary, for the organism to give, at his discretion, to his physician(s).

Example 2 (prophetic example): Determining Predispositions and Risks to Future Human

Children

[00389] A male and female, referred to as 'the couple', is interested in genetic testing to determine diseases or conditions they may pass on their future children. The couple fills out a Carrier Questionnaire. The questionnaire has questions on the medical history as well as the family histories and any known genetic disorders. The questionnaire also asks about any specific diseases that the couple is worried about. The Carrier GC reviews both of their completed questionnaires and writes a brief pre-meeting note, and may complete a genetic pedigree.

[00390] The GC discusses their medical history and reviews their genetic pedigrees, discusses what can and cannot be tested and discusses the limitations of genetic testing as well as the potential insights that may be learned. The GC also talks about some of the most prevalent diseases that are screened for in the various panels, such as Cystic Fibrosis and Type II Diabetes, and some possible implications if the genetic testing is positive or negative for these diseases. The GC explains tests for hundreds of rare genetic disorders are available all at once and provides information about these as well. The GC also explains that even though the couple is primarily interested in diseases and traits that may affect their future children, they may also find out potentially important information about themselves since it is their genetic codes that are being analyzed. The couple agrees to the service and chooses the 'Complete Carrier Package', also known as the Carrier Screening Panel, that investigates hundreds of diseases and traits that the couple could potentially pass on to their child. The GC also explains and reiterates that, at times, carrier genetic testing may also detect disease predispositions that may affect the couple directly and that it is important that they understand this. The couple agrees and may sign a legal waiver and the GC then takes three separate cheek swabs each from the male and female and gives them their respective Confidential Client Numbers, explaining how this is an added safeguard to protect their confidential genetic information so that not even the laboratory may have access to their names. The couple also discusses the cut-off values and their meaning with the GC, and chooses to have all genetic variant-phenotype associations analyzed with a GVP score equal to or greater than 0.5.

[00391] The couple schedules a follow-up appointment in a few days with their same GC. The cheek swab specimens are packaged and shipped overnight to the lab. A few days later the couple's genotype results are transmitted back to the central location and the results are further processed and analyzed to produce a report for their GC, an enhanced report (the Genetic Report) for the couple, and another enhanced report for their physicians (the Healthcare Professional Summary). The GC and the managing physician may review and discuss the reports.

[00392] The report includes the relevant genetic variants and their phenotype associations that were detected, including for the male: genetic variants in the genes HFE, MTTL1, BMP2, and RYR1, and for the female: genetic variants in the genes HFE, MTTL1, BMP2, MTHFD1. The couple meets with their same GC and the managing physician. The GC tells them that they are both carriers of a genetic polymorphism in their HFE gene and that, if they each pass on these genetic variants to their child, the child may have the disease Hemochromatosis. This is an iron-storage disease and can lead to problems with the pancreas, severe liver disease and also liver cancer if not detected and treated properly. The GC explains that because they each have one Hemochromatosis gene, their child has a 25% chance of being likely affected by the disease (which requires both copies of the gene to be present) or a 50% chance of being a carrier or a 25% chance of being neither a carrier nor affected. During the explanation, the GC utilizes a Punnett Square so that the couple can visualize the information (**FIG. 3**). The GC goes on to explain that Hemochromatosis actually has a varied degree of expressivity and penetrance and that even if their child has both abnormal genes, the disease itself may never manifest or, if it does, it may not be detrimental enough to cause any noticeable disease. However, reflex testing determines that they both contain polymorphisms in two other genes, MTTL1 and BMP2, which have both been shown to increase the risk of Hemochromatosis manifesting as a serious disease in organisms who have polymorphisms in the HFE gene, as they do. Therefore, the risk of Hemochromatosis is a possibility for their future offspring.

[00393] Hemochromatosis is a recessive disease, which means that both copies of the gene must be mutated in order for the disease to manifest. The normal gene is usually represented by a capital “H” and the mutated gene, the gene that causes Hemochromatosis, is usually represented by a lower case “h”. However, this Punnett Square has been simplified so that the normal gene is represented by the words “Normal Gene”, also may be represented as “Normal Allele” and the Hemochromatosis gene is represented by words “Disease Gene”, also may be represented as “Disease Allele” in **FIG. 3**.

[00394] As can be visualized by the Punnett Square, for a recessive disease to manifest, one disease gene has to be contributed by the mother and the other disease gene has to be contributed by the father (bottom right square). This shows that there is a 25% chance of their child likely having the disease and a 75% chance of not having the disease (that can be further broken down into the child having a 25% chance of being a non-carrier and 50% chance of being a carrier). These statistics hold for each and every child they have, so there is always a 25% chance of their child likely having Hemochromatosis. This assumes a 100% expressivity and full penetrance, meaning that if the child has both diseased genes (is homozygous for the polymorphism), then the disease always manifests. As explained above in the example and as the genetic counselor would explain to the client, this is not entirely true for many genetic diseases, including Hemochromatosis. The genetic counselor is specially trained in how to properly convey this information to the layperson.

[00395] The GC states that their HFE genetic polymorphism is actually one of the most common human polymorphisms and occurs with a carrier frequency of around 10% of the Caucasian

population and a disease prevalence of approximately 1 in 300 organisms in the US (Merryweather-Clarke, A.T., J Med Genet. 1997 April; 34(4): 275–278 Dr. Hady Sfeir, “Hemochromatosis”, eMedicine Article, www.emedicine.com/MED/topic975.htm, 6/2005). As long as physicians know that a patient has the disease-causing Hemochromatosis polymorphisms, the person can be easily monitored and, if disease manifests, treated by scheduled blood draws in order to decrease the overall iron content of blood.

[00396] The GC recommends that the couple review information available about Hemochromatosis and gives them information about and the web address of the American Hemochromatosis Society (www.americanhs.org). The GC states that, many times organisms with these genetic variants never experience any noticeable disease but, if they do, as long as it is treated, organisms with Hemochromatosis can lead a normal life and have a normal life span. Because of this, the GC may recommend that the couple pursue a routine pregnancy (instead of other fertility options, which include in-vitro fertilization (IVF) with pre-implantation genetic diagnosis (PGD), having an egg or sperm donor, or adoption). If the disease were more serious, such as juvenile onset macular degeneration (which causes irreversible blindness in children), then the GC may have talked more about other options, such as IVF with PGD, which allows for the embryo fertilized in-vitro to be screened for the disease before it is implanted into the uterus.

[00397] The male organism of the couple also has a polymorphism in his RYR1 gene, which means that he is very likely affected with malignant hyperthermia and that their children each have a 50% chance of also having this polymorphism and disease. Malignant hyperthermia is a very serious disease that is triggered by general anesthesia. Therefore, it is important that the male organism inform his primary care physician that he is genetically predisposed to malignant hyperthermia so that this information can be added to his permanent medical record. He is also advised to always inform the surgeon and anesthesiologist of this predisposition if he ever needs surgery for any reason. While malignant hyperthermia can be extremely serious when it manifests, steps can be taken to limit its consequences and avoid serious injury or death as long as the anesthesiologist is made of this predisposition. The vast majority of organisms with this disorder live normal lives and therefore the GC recommends that any children they have get tested for this genetic polymorphisms so that they, too, know if they are predisposed to (or are likely affected by) malignant hyperthermia. The couple is also advised that if, for any reason, their child needs surgery before genetic testing can be conducted, they should inform the anesthesiologist that the father is genetically predisposed to malignant hyperthermia and that the child may be as well. Lastly, the GC explains that his primary care physician may be interested in ordering a simple blood test to measure serum creatine kinase levels, which has shown to be elevated in organisms with this specific polymorphism. All of this information is included in a report that he can give to his physician.

[00398] The female organism is Irish Caucasian and is found to have a homozygous polymorphism in her MTHFD1 gene that has been associated with both an increased risk of having severe abruptio

placentae (in Irish populations) and also with an increased risk of having a child with neural tube defects (in Italian and Irish populations). The managing physician explains what abruptio placentae is and how it may threaten a pregnancy. Her risk of having abruptio placentae is significantly elevated over that of the general population and therefore this is a very important predisposition that her obstetrician may find important and may need to know about. As long as the obstetrician knows to check for this and to educate her about the potential warning signs, then they may be able to institute measures that will actually avoid pregnancy loss if this should occur. Also, due to her having a significantly increased risk over the general population's risk of having a child with a neural tube defect, such as spina bifida, it may be very important that she begins taking daily prenatal vitamins even before she becomes pregnant, since the vitamins are most effective during the first few weeks immediately after conception. Her obstetrician may also want to be made aware of her increased risk of having a child with neural tube defects since many times this can be detected very early in the pregnancy through the use of modern ultra-sound machines and maternal blood tests.

[00399] The genetic counselor continues to review all the other significant findings and also goes over a condensed list of the multitude of genes that did not contain any polymorphisms and they also discuss some of the diseases that they are actually protected against, and that their children may most likely be protected against as well. For instance, the GC tells them that the male organism's genes contain a genetic change that protects him against Alzheimer Disease and that the female's genes contain genetic polymorphisms that protect her against obesity and diabetes.

[00400] The GC gives the enhanced genetic reports to the couple, making sure to give them a copy that they can give to their primary care physician and their obstetrician. The GC tells them that if they would like further genetic counseling, they can schedule that now or anytime in the future.

Example 3 (prophetic): Genetic Profiles for Human Children

[00401] A mother has two children, a boy aged five and a girl aged two. The mother is interested in a special genetic testing panel specifically for children that tests not only for diseases but also certain conditions that may influence a child's learning and development. The mother schedules an appointment for herself and her two children with a Pediatric Genetic Counselor (GC). The Pediatric GC explains to the mother the pediatric genetic testing panel can detect diseases that the children could possibly be afflicted with either now as children or later-on as adults, and also detect disorders that could impede the children's ability to learn and develop properly. For instance, if a gene for obesity is discovered then preemptive modifications such as diet, exercise, and parental oversight may greatly limit the predisposition to gain significant weight. Alternatively, knowing that someone has a genetic predisposition for obesity may actually help that organism come to terms with their weight because it isn't fully in their control. Another example discussed is a gene that controls medication metabolism and what would happen if it is abnormal. In this case, the child may not properly metabolize some medications, which could then cause very high levels of that medication in the blood and this could lead to adverse drug reactions and serious complications.

[00402] After further discussion about what genes are tested for and some of the possible consequences of finding an abnormal gene, the mother agrees to the genetic testing and chooses to have the “Complete Pediatrics Panel”, also known as Pediatric Panel Alpha, run on both of her children. The GC discusses with the mother the different cut-off value options available as well as their meaning, and the mother chooses for a GVP score equal to or greater than 0.5. The GC discusses the implications of allowing genetic variant-phenotype associations with lower GVP scores to be included in the analysis and the mother states that she understands and wants to proceed. The GC then takes cheek swabs of both children and gives the mother their Confidential Client Numbers.

[00403] The mother pays the fee for each child and schedules a follow-up appointment. The GC packages the cheek swab specimens and sends them to the lab. One week later, the results are transmitted electronically and are reviewed by the GC and the managing doctor. Some of the relevant results include genetic variants, such as polymorphisms, in the genes HCRT, ACTN3, HLA-C*0602, and TIRAP detected in the daughter, and the polymorphisms CFTR, MC1R, and DRD4 detected in the son.

[00404] The mother returns and meets with the same GC and the managing doctor. The GC first reviews the daughter’s genetic profile and states that she only has a few non-serious genetic changes.

[00405] 1) Polymorphism in the HCRT gene. Predisposition to Narcolepsy

[00406] The first is a polymorphism in her HCRT gene, which means that she may be predisposed to narcolepsy. The GC explains the symptoms of narcolepsy include excessive sleepiness and possibly falling asleep in situations where most organisms would remain awake (such as while in class or when driving a car). Because of this, the mother should be aware that if her daughter is having difficulty in school or ever shows signs of excessive sleepiness, this could actually be a treatable medical condition and that the daughter should then see a sleep specialist (the GC can refer them to or may give them a list of qualified sleep medicine physicians in their community, if necessary).

[00407] 2) Polymorphism in the ACTN3 gene. This specific genetic polymorphism is associated with elite athletic performance.

[00408] The daughter possesses a genetic polymorphism in the ACTN3 gene that has been associated with exceptional athletic performance. This specific genetic polymorphism promotes much more efficient aerobic muscle metabolism that may allow the daughter to perform physical activities, such as running and swimming, for much longer continuous periods of time (estimated at 33% in some studies) without reaching exhaustion. This polymorphism has been found to be overrepresented in endurance athletes around the world. Because of this, the mother may want to encourage her daughter to participate in endurance-related sports and athletic programs both at school and during the summer.

[00409] 3) HLA-C*0602 detected. Predisposition to Early-onset Psoriasis.

[00410] The GC explains that the daughter contains a specific form of HLA-C, known as *0602, and that this genetic marker has been associated with a very significant increased risk of early-onset psoriasis. This genetic predisposition is important for the mother to be aware of since psoriasis is a

condition that is usually treatable by a dermatologist. Her daughter can receive the proper care right at the onset if the disease manifests, rather than at a later time when emotional and psychological stress may have had a significant impact upon the child. The dermatologist may also be more likely to treat the problem more aggressively right at the onset since her daughter is known to be genetically predisposed to it.

[00411] The managing doctor describes the symptoms of psoriasis and states that there are many different types of treatments available if the disease should manifest.

[00412] 4) Polymorphism in the TIRAP gene. This polymorphism may be associated with protection against serious infectious diseases.

[00413] The daughter has a polymorphism in her TIRAP gene. This polymorphism has recently been shown to confer protection against infectious diseases, such as invasive pneumococcal disease. Because of this, she may actually find that she is more resistant to serious infections than most organisms are.

[00414] The GC and the managing doctor also discuss the son's results with the mother.

[00415] 1) Polymorphism in the CFTR gene.

[00416] The son is a carrier of a cystic fibrosis genetic polymorphism. However, he most likely has one normal gene since only a single genetic polymorphism is detected, so he will most likely not be affected by this disease.

[00417] The fact that he is a carrier of a CFTR genetic polymorphism may be important information for the son to know about when he does decide to marry. When he does decide to start a family, it may be prudent for his wife to also have her CFTR gene tested, if it hasn't been already, in order to ascertain the true risk associated with having a child with cystic fibrosis, which is a very serious illness. By knowing that the son is a carrier of this genetic mutation, he can now be empowered over it potentially creating disease in future generations.

[00418] 2) Polymorphism in the MC1R gene. This specific polymorphism has been associated with red-hair, fair-skin, increased risk of melanoma, and also increased anesthesia requirements during surgical procedures.

[00419] The GC notes the son has red-hair and fair-skin and these traits are mostly likely due to a genetic change that is detected in his MC1R gene. Besides the hair and skin color traits, this genetic change also makes him extra-sensitive to the harmful UV-rays of the sun and increases his risk of developing melanoma. While this may not affect him for many years, melanoma is very deadly and it is important that both his primary care physicians and his dermatologists always know about this predisposition. Because of this, an optional recommendation presented to the mother is that he become acquainted with a dermatologist and receive full-body checks for melanoma on a regular basis. Hopefully, with the knowledge of this predisposition and increased monitoring, any melanoma that develops may be detected and removed from his body very quickly. Increased monitoring due to a known genetic predisposition has the potential to greatly limit the morbidity and high mortality of

this disease. If his predisposition to melanoma was not known, then a suspicious lesion may have been discovered either months or years after it developed, which may then necessitate radical surgery with resultant physical deformity and also a high likelihood of metastatic disease (even after surgical removal) and possibly death.

[00420] The same genetic change in the MC1R gene that predisposes the son to melanoma has also been shown to correlate with increased anesthesia requirements during surgery. If he ever has to have surgery, this may be important information to discuss with the surgeon and anesthesiologist so that they can make sure he receives the proper analgesia and sedation during the entire procedure.

[00421] 2) Polymorphism in the DRD4 gene and other relevant genes detected and these polymorphisms may be associated with Attention-Deficit-Hyperactivity Disorder.

[00422] The GC notes that while the vast number of genes screened for were all normal, the son does have another change in his DRD4 gene, which may predispose to attention deficit hyperactivity disorder (ADHD). The GC describes the symptoms of this disease, stating that some children who have ADHD have significant learning difficulties until this disease is diagnosed and properly treated.

[00423] The GC states that if behavioral or learning issues arise, the son may benefit from seeing a psychiatrist who specializes in ADHD (and the GC can recommend the a list of names of child psychiatrists in her community, if needed). With proper oversight and treatment, it is very likely that the son may do just fine in school if it is found that his trouble concentrating and learning new material is due to this disorder.

[00424] The GC gives the mother a copy of the results and recommendations for both children, as well as referrals to a dermatologist and a pediatric psychiatrist. Additional copies of the reports are included for these doctors and also for the children's pediatrician. The mother is told that the GC would be happy to discuss these results with any of the doctors if they have any questions.

Example 4 (prophetic): Genetic Profile for a Single Human Gene and Human Condition

[00425] An organism has intense pain with breastfeeding her child and wants to switch to formula. Before switching she wants to determine whether breastfeeding may increase her baby's IQ level. A single gene, such as the breastfeeding intelligence gene is tested for in the baby by having a managing physician or the child's pediatrician roll a small q-tip-like swab on the inside of the baby's cheek to obtain a genetic sample.

[00426] The baby is found to contain the gene that may increase her intelligence only if she is breastfed. The physician also states that they can refer the mother to a nurse who specializes in breastfeeding and may be able to assist with some techniques to make it less painful, if the mother decides to continue with breastfeeding.

Example 5 (prophetic): Algorithm for Calculating Predictive Medicine Risk (PMR)

[00427] The following example utilizes the multiplicative model but any algorithm known in the art may also be utilized instead of the multiplicative model, such as the additive model.

[00428] The Greek letters α , β , and γ is used to represent different alleles. For example, these Greek letters may represent nucleotides (adenine, cytosine, guanine, or thymine), such as with single nucleotide polymorphisms where, for example, α may represent a cytosine, β may represent a thymine, and γ may represent an adenine. Alternatively, the Greek letters α , β , and γ may represent alleles of any other type of genetic variant, such as insertions and deletions, for example where α may represent the insertion and β may represent the deletion, or for copy number variations, where α may represent 1 copy, β may represent 2 copies, and γ may represent 3 copies. As can be seen, the Greek letters are used to represent the different possible alleles of any type of genetic variant, such as any type of mutations, SNPs, DIPs, CNVs, translocations, repeats, etc.

[00429] Many genetic variants are biallelic, meaning that there are two possible alleles (Allele α and Allele β) and therefore three possible genotypes: $\alpha\alpha$, $\alpha\beta$, $\beta\beta$. At times, however, genetic variants may have more than two possible alleles. For example, triallelic genetic variants have three possible alleles (Allele α , Allele β , and Allele γ) and therefore six possible genotypes: $\alpha\alpha$, $\alpha\beta$, $\beta\beta$, $\alpha\gamma$, $\beta\gamma$, $\gamma\gamma$. This can be expanded out to include as many alleles and genotype combinations as is necessary to capture all the possible variations at a specific genetic variant. Therefore, while many times there are usually just two alleles and three possible genotypes, there can also be three alleles and six possible genotypes, and there can also be more than three alleles and more than six possible genotypes.

[00430] The following example considers the scenario where two genetic variants and their genotypes have been detected through genetic testing that are associated with risk for phenotype X. While two genetic variants are utilized in this example to convey the application of the algorithm to multiple independent and relevant genetic variants associated with risk for the same phenotype, any number of genetic variants may be used and this algorithm is applicable to any number of genetic variants.

[00431] For this example, two genetic variants (A and B) are detected that are associated with phenotype X, and the genotypes for these two genetic variants are associated with risk for phenotype X.

Genetic variant A is a biallelic SNP with allele 1 = α and allele 2 = β

Genetic variant B is a biallelic SNP with allele 1 = γ and allele 2 = δ

[00432] In this example, results from genetic testing yield the following raw genotypic data for the genetic variants:

[00433] Genetic variant A genotype detected: $\alpha\beta$

Genetic variant B genotype detected: $\delta\delta$

[00434] Note that α , β , γ , and δ are meant to represent different alleles and, as stated above, they can represent any type of allelic variant, such as a nucleotide, an insertion or deletion, a copy number variation, etc. Genetic variants A and B are distinct and represent separate genetic variants that are both associated with and relevant for phenotype X. For example, if genetic variants A and B are both SNPs, genetic variant A's α may represent a cytosine and genetic variant A's β may represent a

thymine while genetic variant B's γ may represent a thymine and genetic variant B's δ may represent a guanine. As stated above, the Greek letters are just meant to represent different possible alleles and each is unique to each specific genetic variant, as described. In the example given, genetic variant A having the $\alpha\beta$ genotype means it is heterozygous for its two alleles and genetic variant B having the $\delta\delta$ genotype means it is homozygous for one of its alleles.

Genetic variant A genotype detected: $\alpha\beta \rightarrow$ risk value $A_{\alpha\beta}$ for phenotype X

Genetic variant B genotype detected: $\delta\delta \rightarrow$ risk value $B_{\delta\delta}$ for phenotype X

[00435] The risk value for each allele or genotype that is associated with each specific genetic variant-phenotype association is ascertained from published studies and published literature, such as journal articles.

Risk Values: OR = Odds Ratio or RR = Relative Risk

[00436] If the risk values for the genetic variants alleles or genotypes (risk value $A_{\alpha\beta}$ and risk value $B_{\delta\delta}$) are given as RRs, then skip to step 2. If the risk value for either or both of the genetic variants and their alleles or genotypes are given as ORs, then proceed to step 1.

[00437] Step 1 – Conversion

Genetic variant A ORs = ($ORA_{\alpha\alpha}$, $ORA_{\alpha\beta}$, $ORA_{\beta\beta}$)

[00438] Genetic variant B ORs = ($ORB_{\gamma\gamma}$, $ORB_{\gamma\delta}$, $ORB_{\delta\delta}$)

Convert ORs to RRs, as described previously herein.

[00439] Genetic variant A RRs = ($RRA_{\alpha\alpha}$, $RRA_{\alpha\beta}$, $RRA_{\beta\beta}$)

[00440] Genetic variant B RRs = ($RRB_{\gamma\gamma}$, $RRB_{\gamma\delta}$, $RRB_{\delta\delta}$)

[00441] Step 2 – Assess allele or genotype frequencies from matched reference population for the allele or genotypes of genetic variants A and B

[00442] Data ascertained from resources as described, such as The International HapMap Project or the National Center for Biotechnology Information (NCBI)'s dbSNP.

Allele Frequency (AF) of genetic variant A = AFA_{α} , AFA_{β}

Allele Frequency (AF) of genetic variant B = AFB_{γ} , AFB_{δ}

Genotype Frequency (GF) of genetic variant A = $GFA_{\alpha\alpha}$, $GFA_{\alpha\beta}$, $GFA_{\beta\beta}$

Genotype Frequency (GF) of genetic variant B = $GFB_{\gamma\gamma}$, $GFB_{\gamma\delta}$, $GFB_{\delta\delta}$

[00443] Step 3 – Calculate Cumulative Generic Population Risk Load (GPL)

GPL for genetic variant A = $GPL_A = ((RRA_{\alpha\alpha}) \times (GFA_{\alpha\alpha})) + ((RRA_{\alpha\beta}) \times (GFA_{\alpha\beta})) + ((RRA_{\beta\beta}) \times (GFA_{\beta\beta}))$

GPL for genetic variant B = $GPL_B = ((RRB_{\gamma\gamma}) \times (GFB_{\gamma\gamma})) + ((RRB_{\gamma\delta}) \times (GFB_{\gamma\delta})) + ((RRB_{\delta\delta}) \times (GFB_{\delta\delta}))$

Cumulative GPL for phenotype X for genetic variants A and B = $GPL_{xc} = (GPL_A) \times (GPL_B)$

[00444] Step 4 – Calculate the organism's Proband Risk Load (PRL)

[00445] The PRL is based on the relative risks associated with the specific detected allele or genotype for each genetic variant. In this example, the PRL is calculated from genetic variant A (detected genotype = $\alpha\beta$) and from genetic variant B (detected genotype = $\delta\delta$).

PLR for Phenotype X = $PRL_x = (RRA_{\alpha\beta}) \times (RRB_{\delta\delta})$

[00446] Step 5 – Calculate the Cumulative Genetic Risk (CGR)

CGR for Phenotype X = $CGR_x = PRL_x / GPL_{xc}$

[00447] Step 6 – Calculate the Predictive Medicine Risk (PMR)

[00448] The generic gender-specific population lifetime risk percent (GLR) for phenotype X (GLR_x) is ascertained from literature and resources as previously described herein.

PMR for Phenotype X = $PMR_x = (CGR_x) \times (GLR_x)$

[00449] (The upper bound for the PMR of multifactorial phenotypes may be set at an upper limit, such as 95%, as these phenotypes may not be fully determined by genetic factors alone. The lower bound for the PMR of multifactorial phenotypes may be set at a lower limit, such as 0.0001%, as these phenotypes may not be fully determined by genetic factors alone.)

Example 6 (prophetic): Organ System Score and Overall Genetic Health Score

[00450] A 35 year old Caucasian female smoker 20 lbs overweight for her age and height, presents for genetic testing and chooses the Executive Platinum Package, also known as the Executive Panel Alpha. Relevant information is obtained from the organism, entered into a system, and utilized during analysis. The information includes the organism's gender, age, premenopausal state, ethnicity, smoking habit, weight information, family history of no breast cancer, and testing panel request for the Executive Platinum Package of having thousands of clinical polymorphisms analyzed.

[00451] A raw polymorphism data chart for the organism is generated (for example, **Table 13**). The SNP-Disease Coefficient Rating (SDCR), also known as the GVP score, is obtained by analyzing studies determining the correlation between a genetic variant, such as a SNP, and a phenotype, such as a disease or trait. The Generic Absolute Risk (GAR), also known as the GLR, is determined from published literature while the Cumulative Genetic Risk (CGR) may include information such as Risk Values, expressed as an odds ratio (OR), relative risk (RR) or hazard ratio (Z). The Cumulative Genetic Risk (CGR) is determined by incorporating all the relevant SDCs (SNP-Disease Coefficients, also known as the GVP score) applicable to a specific disease or condition, based on selected cut-off threshold values. For example, for a disease X, polymorphisms A and B are detected, where A has an OR_1 and B has an OR_2 . Utilizing HapMap data for the reference population (such as CEU HapMap data for a Caucasian or European American population), genotype frequencies for each of the two alleles (Allele1 and Allele2) or each of the three genotype possibilities (Allele1/Allele1, Allele1/Allele2, and Allele2/Allele2), as there are usually three genotype possibilities, such as with biallelic SNPs, although there may be more genotype possibilities, such as with triallelic SNPs, as discussed in **Example 5**, for each of the genetic variants can be ascertained and these may then be

multiplied by the risk value (RV), such as relative risks, for each of the respective allele or genotypes for that same genetic variant and specific phenotype, such as disease, association and these values (taking into account all the possible allele or genotypes, the frequency in the population for each allele or genotype added or multiplied, depending on whether an additive or multiplicative or other methodology is used, by the allele or genotype risk value for each of the genetic variant's alleles or possible genotypes) may then all be added together for each of the genetic variant to give the cumulative generic population risk load (GPL) for each genetic variant and then the GPLs for each other genetic variants (A and B) may be multiplied together to give the cumulative generic population risk load (GPL_c) while the CGR for disease X would be $RV_1 + RV_1$ or $RV_1 \times RV_2$, such as $OR_1 + OR_2$ or $OR_1 \times OR_2$ or $RR_1 + RR_2$ or $RR_1 \times RR_2$, (depending on whether the additive or multiplicative or other methodology is used) divided by the GPL_c . If the prevalence of the phenotype is high (for example, greater than 10%), then the odds ratios may be converted to relative risks first and then either added together or multiplied together as before, again depending on whether the additive or multiplicative methodology is utilized. If no risk value (NRV) is available, a placeholder risk can be assigned by a physician or genetic counselor or bioinformatics specialist analyzing the organism's genetic profile. A Predictive Medicine Risk (PMR) can be determined by, in one iteration, relating back to the previous models multiplying the GAR, also referred to as the GLR, by the CGR or in another iteration methodology relating back as stated by adding the GAR, also referred to as the GLR, with the CGR depending on the methodology, GAR, prevalence, and incidence of the specific multifactorial phenotype, such as disease, that is being analyzed at that time. A Clinical Significance Rating (CSR) can also be determined, where 0 would indicate no clinical use, 1 would indicate limited clinical significance, value, or use, 2 would indicate moderate clinical significance, 3 would indicate very useful in a clinical setting, where a medical professional would likely find the result valuable, and 4 would indicate extreme clinical significance, possibly relating to a life-threatening condition. The DIR, or Disease and Trait Impact Rating, also referred to as the PIR, indicates the severity of a phenotype that is correlated with a genetic profile. For example, the DIR ranges from -3 to +3, where -3 causes sudden death or debilitating disease, -2 indicates a serious disease, a disease or condition that is difficult to cure, may cause death, or has significant negative life consequences, -1 indicates a condition that is usually manageable, 0 is a neutral condition or trait, +1 a slightly positive impact; +2 is a helpful trait, and +3 is a provides a significant advantage to the organism.

[00452] The CGR Multiplier and PMR (Predictive Medicine Risk) or NRV (No Risk Value) Multiplier is chosen (see for example **FIG. 9**), as is the CSR (Clinical Significance Rating) and the DIR (Disease and Trait Impact Rating also known as the Phenotype Impact Rating or PIR) and the NMF (Notice Me Factor). The Action Score (AS) may be determined by multiplying the SDCR, CGR Multiplier, PMR or NRV Multiplier, CSR and DIR or by multiplying the CSR, DIR, and NMF, or the CSR, PIR, and NMF. The Cumulative Action Score (CAS) may be determined by adding all the AS's for all of the phenotypes, such as diseases or traits, that fall under the same organ system,

which may also be identified by medical specialty and then dividing by the total number of AS's, The Cumulative Action Score may therefore be the average action score for that organ system, which can also be identified by medical specialty. Each of the organism AS's is already weighted in terms of clinical significance, degree of phenotype benefit or harm, and significance of the change in risk, as previously discussed.

[00453] A chart for scores by organ system and an overall genetic health score can be used, such as shown in **FIG. 10**. The Cumulative Action Score (CAS) can be filled in for more than one organ system and determined for an organ system. The organ system score or Indicator of Genetic Health of an Organ System can be indicated by a color. Red would be used for scores less than -10, indicating highly important to discuss with client and may be highly important for client to follow-up with their physician or specialist based on this information, pink can be used for scores between -1 to -10 to indicate moderately important risk, green can be used for scores of 0 to indicate no pertinent deleterious or protective information discovered although organ system was accessed, blue can be used for scores between +1 to +10, to indicate moderately important protection, gold can be used for scores >+10 indicating very beneficial protection, and no color can be used for an Organ System or Medical Specialty if it was not accessed. The overall genetic health score can be determined, as described above, by adding all the CAS, which may be used as an indicator for genetic wellness and is also represented by a color as is the Indicator of Genetic Health of an Organ System, and dividing by the total number of CAS's, as previously described

[00454] Selected raw polymorphisms data is shown in **Table 13**.

Table 13: Selected Raw Polymorphism Data

Oncology & Women's Health	
Polymorphism in LOC643714	
Locus 16q12	
SNP Identifier: rs3803662	
Genotype: TT	
Clinical Correlation: Breast Cancer, Estrogen-receptor Positive	
Odds Ratio: 1.64	
*SNP-Disease Coefficient =	
Population: Caucasian	
Polymorphism in Intergenic Region	
Locus 2q35	
SNP Identifier: rs13387042	
Genotype: AA	
Clinical Correlation: Breast Cancer, Estrogen-receptor Positive	
Odds Ratio: 1.44	
SNP-Disease Coefficient =	
Population: Caucasian	
Polymorphism in MAP3K1	
Locus 5q11.2	

SNP Identifier: rs889312
Genotype: CC
Clinical Correlation: Breast Cancer
Odds Ratio: 1.27
SNP-Disease Coefficient =
Population: Caucasian
Polymorphism in TNRC9
Locus 16q12.1
SNP Identifier: rs3803662
Genotype: TT
Clinical Correlation: Breast Cancer
Odds Ratio: 1.39
SNP-Disease Coefficient =
Population: Caucasian
Oncology & Women's Health
Polymorphism in FGFR2
Locus 10q26
SNP Identifier: rs1219648
Genotype: GG
Clinical Correlation: Breast Cancer
Odds Ratio: 1.64
SNP-Disease Coefficient =
Population: Caucasian, Post-menopausal Women
Pharmacology & Oncology
Polymorphism in CYP19A1
Locus 15q21.1
o SNP Identifier: rs4646
o Genotype: CA
o Clinical Correlation: Improved Treatment Efficacy of Aromatase Inhibitor Letrozole in Advanced Breast Cancer, Estrogen-receptor Positive
o Hazard Ratio: 0.52
SNP-Disease Coefficient =
o 17.2 months to breast cancer disease progression with genotype CA or AA and Letrozole versus 6.4 months to disease progression with genotype CC and Letrozole
SNP-Disease Coefficient =
o Population: Post-menopausal Women with Estrogen-receptor Positive Breast Cancer
Polymorphism in MDM2
o Locus: 12q14.3-q15
o SNP Identifier: rs2279744
o Genotype: GG
o Clinical Correlation: Resistance to Topoisomerase II-Targeting Chemotherapeutic Drugs (Etoposide, Mitoxantrone, Amsacrine, and Ellipticine)
SNP-Disease Coefficient =

Polymorphisms <i>not</i> detected in RAD51 & XRCC3
o Loci: 15q15.1 & 14q32.3
o Haplotype Identifier: rs1801320 & rs861539
o Haplotype: G-T
o Clinical Correlation: This haplotype is associated with over a 700% increased risk of developing chemotherapy-related AML (Acute Myelogenous Leukemia), a type of blood cancer.
SNP-Disease Coefficient =
Endocrinology & Traits
Polymorphism in APOB
o SNP Identifier: rs679899
o Locus: 2p24
o Genotype: CC
o Clinical Correlation: Increased BMI with Smoking
SNP-Disease Coefficient =
Cardiovascular & Hematology
Polymorphism in FGB
Locus 4q28
SNP Identifier: rs1800790
Genotype: GA
Clinical Correlation: Increased Plasma Fibrinogen Levels
SNP-Disease Coefficient =
Population: Caucasian
Polymorphism in MTHFR
Locus 1p36.3
SNP Identifier: rs1801133
Genotype: TT
Clinical Correlations:
Decreased Longevity
SNP-Disease Coefficient =
Hyperhomocysteinemia, Neutralizable with Folate Supplementation
SNP-Disease Coefficient =
Increased risk of Premature Cardiovascular Disease
Odds Ratio = 3.00
SNP-Disease Coefficient =
Increased risk of Ischemic Stroke
Odds Ratio = 1.24
SNP-Disease Coefficient =
Increased risk of Neural Tube Defect
Odds Ratio = 7.20
SNP-Disease Coefficient =
Increased risk of Pulmonary Embolism with Oral Contraceptive Pills
SNP-Disease Coefficient =
Increased risk of Thrombosis with Smoking
SNP-Disease Coefficient =
Increased risk of Preeclampsia
SNP-Disease Coefficient =
Mother at Increased Risk of Having a Child with Down Syndrome
Odds Ratio = 1.91
SNP-Disease Coefficient =

Increased risk of Primary Open-angle Glaucoma
Odds Ratio = 2.38
SNP-Disease Coefficient =
Increased risk of Migraine with Aura
Odds Ratio = 2.05
SNP-Disease Coefficient =
Increased risk of Depression
Odds Ratio = 1.69
SNP-Disease Coefficient =
Increased risk of Schizophrenia
Odds Ratio = 1.48
SNP-Disease Coefficient =
Increased Need for B-vitamin Nutritional Supplementation
SNP-Disease Coefficient =
Population: Caucasian
Cardiovascular & Hematology
Polymorphism in F5
Locus 1q23
SNP Identifier: rs6025 (Factor V Leiden Mutation)
Genotype: AA
Clinical Correlations:
Increased risk of Venous Thromboembolism
Odds Ratio = 18.00, Lifetime Risk = 10%
SNP-Disease Coefficient =
Increased risk of Thrombosis if Nonsmoker, Normal Weight, Under 40 y/o
10-year Absolute Risk = 3%
SNP-Disease Coefficient =
Increased risk of Thrombosis if Smoker, Overweight, Over 60 y/o
10-year Absolute Risk = 51%
SNP-Disease Coefficient =
Increased risk of Deep Vein Thrombosis Recurrence after First DVT
Odds Ratio = 2.94
SNP-Disease Coefficient =
Increased risk of Late Fetal Loss when Pregnant
Odds Ratio = 3.00
SNP-Disease Coefficient =
Increased risk of Thromboembolism with Pregnancy
Odds Ratio = 9.30
SNP-Disease Coefficient =
Significantly Increased risk of Thromboembolisms if on Oral Contraceptive Pills
SNP-Disease Coefficient =
Population: Caucasian
Polymorphism in F7
Locus 13q34
SNP Identifier: rs6046
Genotype: TT
Clinical Correlations:
Factor VII Deficiency
Protection against Myocardial Infarction
Odds Ratio = 0.47
SNP-Disease Coefficient =

Increased risk of Recurrent Venous Thrombosis
Odds Ratio = 1.30
SNP-Disease Coefficient =
Population: Caucasian
Polymorphisms detected in FGB, MTHFR, F5, and F7
Loci: 4q28 & 1p36.3 & 1q23 & 13q34
Haplotype Identifier: rs1800790 & rs1801133 & rs6025 & rs6046
Haplotype: A-T-A-T
Clinical Correlation: Increased risk of Recurrent Venous Thrombosis
Odds Ratio = 5.10
SNP-Disease Coefficient =
Population: Caucasian
Pharmacology & Cardiovascular
Polymorphism in VKORC1
Locus 16p11.2
SNP Identifier: rs9923231
Genotype: AA
Clinical Correlation: Increased Sensitivity to Warfarin (Coumadin)
SNP-Disease Coefficient =
Population: All
Polymorphism in KIF6
Locus 6p21.2
SNP Identifier: rs20455
Genotype: TC
Clinical Correlations:
Increased risk of Coronary Artery Disease
Odds Ratio = 1.24 (Caucasian Female)
Odds Ratio = 1.50 (Caucasian Male)
SNP-Disease Coefficient =
High-dose Atorvastatin Therapy (80mg) Reduced Risk of Death or Major Cardiovascular Events by 41% Compared with Standard-dose Pravastatin Therapy
Hazard Ratio = 0.59
SNP-Disease Coefficient =
Polymorphism in KCNE2
Locus 21q22.1
SNP Identifier: eg2525
Genotype: GC
Clinical Correlations:
Drug (Clarithromycin) Induced Long QT Interval and Cardiac Ventricular Arrhythmias
SNP-Disease Coefficient =
Population: Caucasian
WARNING: Potential fatal interaction with Clarithromycin. Avoid clarithromycin. Educate organism about this potential fatal interaction. Make sure medical records clearly highlight this potential fatal interaction.
Cardiovascular
Polymorphism in AGT

Locus 1q42-q43
SNP Identifier: rs699
Genotype: CC
Clinical Correlations:
Increased risk of Salt-Sensitive Hypertension
SNP-Disease Coefficient =
Increased risk of Pregnancy-Induced Hypertension
SNP-Disease Coefficient =
Population: Caucasian
“Using organismized dose adaptation, a significant reduction of bleeding complications can be expected, especially in the initial drug saturation phase. Furthermore, concomitant application of low dose vitamin K may significantly reduce intra-organism coumarin dose variation and, thus, may stabilize oral anticoagulation therapy. The use of new pharmacogenetics-based dosing schemes and the concomitant application of low-dose vitamin K with coumarins will decidedly influence the current practice of oral anticoagulation and greatly improve coumarin drug safety.” (Oldenburg, J. Thromb Haemost. 2007 Sep;98(3):570-8.
Rheumatology
Polymorphism in GDF5
Locus 20q11.2
SNP Identifier: rs143383
Genotype: CT
Clinical Correlations:
Osteoarthritis of the Hip & Knee
Odds Ratio = 1.28 (Caucasian)
Odds Ratio = 1.79 (Chinese & Japanese)
SNP-Disease Coefficient =
Decreased Height (Standing Height)
SNP-Disease Coefficient =
Endocrinology & Traits
Polymorphism in FTO
Locus 16q12.2
SNP Identifier: rs9939609
Genotype: AA
Clinical Correlations:
Increased risk of being overweight during childhood
Odds Ratio = 1.27
SNP-Disease Coefficient =
Increased risk of obesity during childhood
Odds Ratio = 1.35
SNP-Disease Coefficient =
Increased risk of being overweight during adulthood
Odds Ratio = 1.38
SNP-Disease Coefficient =
Increased risk of obesity during Adulthood
Odds Ratio = 1.67
SNP-Disease Coefficient =
Significant Increased in Weight Over 25-years Starting in Youth
SNP-Disease Coefficient =

Diabetes Mellitus, Type II due to Increased Obesity from this Gene
Odds Ration = 1.55
SNP-Disease Coefficient =
Population: Caucasian
Polymorphism Level = -1
Endocrinology & Traits
Polymorphism in TUB
Locus 11p15.5
SNP Identifier: rs2272382
Genotype: AA
Clinical Correlations:
Increased risk of obesity during Adulthood
Odds Ratio = 1.32
SNP-Disease Coefficient =
Diet found to Contain Increased Glycemic Load
SNP-Disease Coefficient =
Derive Less Energy from Fat in Diet
SNP-Disease Coefficient =
Population: Caucasian
Hematology
Polymorphism in ABO
Locus 9q34
DIP Identifier: eg22696
Genotype: deletion/deletion
Clinical Correlation: Blood Type = O
SNP-Disease Coefficient =
Population: Caucasian
Polymorphism Level = 0
Pharmacology
Polymorphism in CACNA1S
Locus 1q32
SNP Identifier: eg36558
Genotype: GA
Clinical Correlation: Malignant Hyperthermia
SNP-Disease Coefficient =
WARNING: Extreme caution with general anesthesia. Educate organism about that they may be genetically predisposed to malignant hyperthermia. Reiterate the importance of informing all physicians, especially anesthesiologists and surgeons, about this predisposition. Make sure this predisposition appears clearly in their medical record.
Traits & Psychiatry
Polymorphism in GABBR2
Locus:
SNP Identifier:
Genotype:
Clinical Correlations: Increased risk of Nicotine Addiction

SNP-Disease Coefficient =
Population: Caucasian
Traits & Psychiatry
Polymorphism in CYP2B6
Locus: 19q13.2
Haplotype Identifier: rs3745274 & rs2279343
Haplotype: TT-GG
Clinical Correlations:
Indicator of Bupropion Success for Treatment of Nicotine Addiction (Abstinence at 10 Weeks & Six Months)
Odds Ratio = 2.97
SNP-Disease Coefficient =
Reduced Dosage required with Efavirenz
SNP-Disease Coefficient =
Population: Caucasian
Ear, Nose and Throat & Pharmacology
Polymorphism in MTRNR1
Locus: Mitochondrial DNA
SNP Identifier: eg1555
Genotype: AG
Clinical Correlations:
Deafness caused by exposure to Aminoglycosides (a class of antibiotics)
SNP-Disease Coefficient =
Late-onset Sensorineural Deafness
SNP-Disease Coefficient =
Population: All
WARNING: Avoid all aminoglycosides. Refer to ENT specialist due to the possibility of developing late-onset sensorineural deafness. Educate organism about importance of avoiding aminoglycosides for their entire life and about the possibility about late-onset deafness. Recommend for organism's extended family members to be tested for the mutation along the maternal lineage so that they, too, will know whether they need to strictly avoid all aminoglycosides.
Discuss with organism the symptoms of restrictive cardiomyopathy and that if any symptoms manifest, they should seek medical attention. Physicians should have low threshold for pursuing cardiomyopathy work-up if organism presents with any symptoms. Start therapy sooner rather than later.
Gastroenterology & Pharmacology
Polymorphism in TPMT
Locus 6p22.3
SNP Identifier: eg55417
Genotype: CA
Clinical Correlation: Possible susceptibility to 6-mercaptopurine Toxicity
SNP-Disease Coefficient =

WARNING: 6-MP (Mercaptopurine) and Azathioprine Toxicity. This is a very important detection for this organism because they are predisposed to Crohn Disease, and Azathioprine or 6-MP are often used as part of the medical treatment. Organism should be educated about this sensitivity and it should clearly annotated on their medical records. Organism should be instructed to discuss this sensitivity with their gastroenterologist, as it will be important if they are ever diagnosed with Crohn Disease.
Metabolic and Rare Diseases & Ear, Nose, and Throat
Polymorphism in SLC26A4
Locus 7q31
SNP Identifier: eg25662
Genotype: AC
Clinical Correlation: Carrier of Pendred Syndrome
SNP-Disease Coefficient =
Population: All
Pendred syndrome is the most common form of deafness and is associated with developmental abnormalities of the cochlea, sensorineural hearing loss, and diffuse thyroid enlargement (goiter). This organism is a carrier of the most common mutation causing Pendred syndrome. They should be educated that, because it is a recessive disease, they will not be affected by this mutation. However, this will be important to discuss further when they are thinking about having children. At that time, the other parent of their child should also have their SLC26A4 gene checked for mutations so as to properly ascertain risk of their child having Pendred syndrome.
Metabolic and Rare Diseases
Polymorphism in HEXA
Locus 15q23-q24
DIP Identifier: eg27487
Genotype: Insertion/Deletion
Clinical Correlation: Carrier of Tay Sachs Disease
SNP-Disease Coefficient =
Population: All
Tay-Sachs disease is an autosomal recessive progressive neurodegenerative disorder which, in the classic infantile form, is usually fatal by age 2 or 3 years old. This organism is a carrier of the most common mutation causing Tay Sachs. They should be educated that, because it is a recessive disease, they will not be affected by this mutation. However, this will be important to discuss further when they are thinking about having children. At that time, the other parent of their child should also have their HEXA gene checked for mutations so as to properly ascertain risk of their child having Tay Sachs.
Polymorphism in MUT
Locus 6p12.3
SNP Identifier: eg33094
Genotype: AT
Clinical Correlation: Carrier of Methylmalonic Aciduria
SNP-Disease Coefficient =
Population: All

Methylmalonic aciduria is an autosomal recessive metabolic disorder that has a wide clinical spectrum, ranging from a benign condition to fatal neonatal disease. This organism is a carrier of the most common mutation causing Methylmalonic Aciduria. They should be educated that, because it is a recessive disease, they will not be affected by this mutation. However, this will be important to discuss further when they are thinking about having children. At that time, the other parent of their child should also have their MUT gene checked for mutations so as to properly ascertain risk of their child having Methylmalonic Aciduria.
Polymorphism in COL7A1
Locus: 3p21.3
SNP Identifier: eg7491
Genotype: CA
Clinical Correlation: Carrier of Epidermolysis Bullosa Dystrophica
SNP-Disease Coefficient =
Population: All
Epidermolysis Bullosa Dystrophica, which may be autosomal recessive or autosomal dominant, is a dermatologic disorder that causes severe blistering and scarring, sometimes with resulting disfigurement and significantly increased risk of infection. Due to involvement of the esophagus, malnutrition can occur. Organisms are also at an increased risk for skin cancer. The majority of organisms with this disease die before the age of 30.
Traits
Polymorphism in 40 SNPs (used as Universal Identifier)
Loci: 40 distinct loci throughout genome
SNP Identifiers: x40
Genotype: (40bp Genotype)
Clinical Correlations: Universal Identifier (no disease-associations for any SNP)
SNP-Disease Coefficient =
Population: All
This represents a 'genetic fingerprint' of the organism and no other organism on the planet will have the same universal identifier. In all populations, the probability of discrimination is greater than 0.999999999999. This is useful as a way to identify the organism, or as life-long security method to always be able to identify a newborn, child, head of state, person in the military, person under investigation or watch, or high profile organism, such as an executive of a large corporation.
Polymorphism in (ETHNICITY)
Locus: 2q21
SNP Identifier:
Genotype:
Clinical Correlations:
Population:
SNP-Disease Coefficient =

[00455] *SNP-Disease Coefficient: 0 = Two or more contradictory studies; 0.25 = Single study with single study population containing under 250 organisms; 0.50 = Single study with single study population containing over 250 organisms; 0.75 = Single study with two or more study populations with each containing under 250 organisms; 1 = Monogenic disorder; polymorphism found to segregate with disease or found within gene that has previously been associated with disease or likely

to be associated with disease; 1 = Single study with two or more study populations (same or different ethnicities), each containing 250-999 organisms and each giving similar results; 1.25 = Single study with two or more study populations (same or different ethnicities), each containing over 1,000 organisms and each giving similar results; 1.50 = One primary study and one replication study, each with similar findings (same disease association and same direction of risk); 1.75 = One primary study with two or more replication studies, each with similar findings (same disease association and same direction of risk); 2 = Two or more GWAS with similar results.

[00456] A report for the organism can include anonymous organism information with relevant factors (FIG. 4A) and a score report for organ system(s), overall genetic health score (for example, with information derived as shown in FIG. 9, 10). The report for the organism may include the following:

[00457] **Organism Summary:** While no polymorphisms are detected in the primary high-risk but low frequency genetic variants associated with breast cancer (in the BRCA1 and BRCA2 genes), five breast cancer associated genetic variants are detected throughout your genome. This increases your risk of breast cancer significantly. (Odds ratios are be added or multiplied together for a total odds ratio, or converted to relative risks depending on the disease prevalence or incidence statistics, as previously discussed) with a genetic predisposition towards estrogen-receptor positive breast cancer.) Without any risk factors, your lifetime risk of breast cancer is approximately 7-13%. With these genetic risk factors, your personalized lifetime risk of breast cancer is increased, and may be as high as approximately 24%. The majority of the risk for you exists after the age of 40.

Recommendations or Preventive Measures:

[00458] *Follow-up:* Due to your significantly increased risk of breast cancer based on the genetic analysis conducted, it is recommended that you follow-up with a women's health breast cancer specialist that may be able to discuss potential preventive measures. Due to your increased risk, it may be important for you to visit with this specialist at least once a year in order to monitor for signs of the disease.

[00459] *Screening:* Research has shown that increased radiation to the chest may further increase the risk of breast cancer in organisms who have genetic variants predisposing them to breast cancer. Because of this, you may try to avoid chest x-rays, mammograms, ct-scans, and any other type of radiation whenever possible, but always consult with your physician. Instead, radiologic screening with non-radiologic devices, such as MRI's or Ultrasounds may be warranted.

[00460] *Modifications:* A) Smoking cigarettes has been shown to increase the risk of many different types of cancer, including breast cancer, so it is recommended that you discuss this with your physician and consider quitting smoking. B) The medication Bupropion (Zyban) has been shown to increase some organisms's ability to quit smoking. Based on your specific genetic profile, you are almost 200 times more likely to quit smoking if you use Burpropion. You should discuss this medication along with a plan to quit smoking with your primary care physician. C) Being overweight has also been shown to increase the risk of breast cancer so it is recommended that you

may also want to consider losing weight, such as between 10 to 20 pounds. D) You do have one or more genetic variants that preliminary evidence suggests may cause you to gain weight if you smoke. Therefore, quitting smoking may significantly help with weight loss in the long-run.

[00461] Medications: Because you are predominantly predisposed to estrogen-receptor breast cancer, it is recommended that you discuss this with your physician and that you may want to discontinue any oral contraceptive pills and, later in life, avoid hormone replacement therapy which may be given if you are experiencing severe symptoms during menopause. A) Genetic variants have been detected that may affect the way your body responds to some medications used to treat breast cancer. (Please discuss this information with your physician before you start or stop any medications.) B) It is found that you may be resistant to Topoisomerase II-Targeting Chemotherapeutic Drugs such as Mitoxantrone and therefore this medication may have limited efficacy for you in treating breast cancer. C) It is found that, based on a specific genetic variant, you may respond very well to the Aromatase Inhibitor Letrozole. D) If chemotherapy for breast cancer is required, based on the current genetic analysis, you are not at an increased risk for chemotherapy-induced leukemia (AML), which is a type of cancer of the blood that some organisms get as a serious side effect of their initial chemotherapy treatment for cancer.

[00462] Score By Organ System (assuming all other SNPs tested are not associated with disease): Cardiovascular Score: Green; Dermatology Score: Green; Eyes, Ears, Nose, Throat Score: Green; Obstetrics: Green; Oncology: Red; Pharmacology: Yellow; Women's Health Score: Red; Urology: Green.

Overall Genetic Health Score: Yellow

[00463] Clinician Summary: Based on genetic testing and analysis conducted and based on current literature, organism is at significantly increased risk of breast cancer, possibly having greater than a 20% lifetime risk of breast cancer if the odds ratios for all of her breast cancer-associated genetic variants are converted to relative risks, analyzed and multiplied together (they may also be added together, with the decision based on methodology used to determine multifactorial risk. For further information about algorithm used in this analysis, please contact us or read the section of the summary that discusses the algorithm methodology). The organism has a predisposition towards estrogen receptor-positive breast cancer. A) Genetic profile indicates Bupropion may significantly help this organism to quit smoking. B) If chemotherapy for breast cancer becomes necessary: i) Aromatase Inhibitors may be more effective. ii) Topoisomerase II-Targeting Chemotherapeutic may be less effective. iii) Organism is not be at an increased risk of chemotherapy-induced AML.

Example 7 (prophetic): Organ System Score and Overall Genetic Health Score with More Subject Information

[00464] An organism with information as shown in **FIG. 4B** chooses the Full Genome Analysis Panel to determine her risk or predisposition to a number of phenotypes, such as traits. Raw genotypic data is generated, such as shown in **FIG. 5**, from an internal or outside source, such as genetic testing

conducted at a CLIA-certified laboratory. This data is then entered into the information technology system and preliminary analysis is conducted that associates the specific genetic variants and their specific genotypes with phenotypes, by cross-referencing a database, such as the Predictive Medicine Database, and may then also calculate risk or carrier status again by cross-referencing a database, such as the Predictive Medicine Database. As can be seen in **FIG. 6A-D**, the data can be viewed many different ways, such as without any filters (Results View = All, **FIG. 6A**), with the results filtered by GVP score (Results View = GVP Score ≥ 1.5 , **FIG. 6B**), or the results filtered by only monogenic diseases (Results View = Monogenic, **FIG. 6C**), or the results can also be filtered by more than one field, such as results filtered by specific replication status or those that are monogenic (Results View = Replicated or Monogenic, **FIG. 6D**). This allows for complete operator control over viewing the preliminary associations detected, and allows for the preliminary results to be filtered by any field, either manually or automatically (for example, if preset when the panel was ordered). The Results View = Phenotypes, **FIG. 6E-G**, allows for the viewing of all the phenotypes detected along with the various phenotype rating scales and their associated organ systems and medical specialties. Phenotypes can further be filtered, if necessary, based on any of these fields. After the data is filtered, it is then fully analyzed and a genetic report is produced.

Example 8 (prophetic): Preventive Measures (PMs) based on Preventive Medicine

Recommendations or Interventions (PMRI's) for the Human Disease Alzheimer's Disease

[00465] An organism's genotypic profile or phenotypic profile or both indicates that he or she is at an increased risk for Alzheimer's Disease and specifically contain the APOE-E4 genetic variant, then preventive measures (PMs), based on clinical and scientific research concerning preventive medicine recommendations and interventions (PMRI's) related to the prevention, and delaying the onset, of Alzheimer's Disease may be included in the Genetic Report. PMs based on PMRI's appear in **FIG. 12** under the "Prevention" heading. For example, organisms carrying the APOE-E4 genetic variant are at significantly increased risk of Alzheimer's Disease if they experience a traumatic brain injury. A PM based on a PMRI specific for APOE-E4 carriers states this association and recommends the risk of head injury may want to be avoided, such as by avoiding contact sports and by wearing a protective helmet while bike riding, skate boarding, roller blading, or any other sport where head trauma is a possibility. (*Plassman et al. Neurology 55(8): 1158-1166 (2000)*; *Koponen et al. Neurology 63(4): 749-750 (2004)*)

[00466] Two Genetic Reports are generated, one for the organism and the other for a physician, which contains PMs based on PMRI's that are specifically tailored for each. For example, the PM based on the PMRI for the patient may include a statement similar to "modern brain scans now enable physicians to non-invasively detect the early signs of Alzheimer's disease in a person's brain and to also follow the progression of the disease" while the PM based on the PMRI for the physician may include a statement similar to "FDDNP-PET brain scans are available from UCLA Medical Center in

Los Angeles, California and now provide for a way to detect the development and progression of plaques and tangles in the brain”.

[00467] The PMs based on the PMRIs for both Genetic Reports further may include one or more of the following types of information:

[00468] A) Disease Education: Description of Alzheimer’s disease, such as its cause, pathology or presentation.

[00469] B) Disease Warning Signs and Symptomatology:

[00470] A description of symptoms of Alzheimer’s disease, such as it being a degenerative and terminal disease that affects a person’s memory, cognition, and mood.

[00471] Symptomatology may be referenced based on a scale, such as time. For example, memory loss may be an initial symptom early on in the course of the disease while increased impairment in learning, and possibly language, occurs at a later stage.

[00472] Examples of symptoms that may indicate that the organism should consult with their healthcare provider include cognitive issues that may first start to manifest during daily activities, such as repeatedly misplacing car-keys or a decreasing ability to balance a checkbook.

[00473] C) Modifications

[00474] Increasing physical exercise (such as walking the golf course instead of using the golf cart, or taking walks after lunch or dinner) (*Larson et al. Ann Intern Med 144(2): 73-81 (2006)*)

[00475] Increasing mental exercise (such as playing chess, learning a new language, or doing a daily crossword puzzle) (*Willis et al. JAMA 296(23): 2805-2814 (2006)*)

[00476] Protecting your head from any type of trauma (such as if a child is considering whether or not to participate in a contact sport such as ice hockey) (*Plassman et al. Neurology 55(8): 1158-1166 (2000); Koponen et al. Neurology 63(4): 749-750 (2004)*)

[00477] Drinking coffee, even up to three or more cups per day. Reflex testing shows that caffeine consumption during the day should not have a negative affect upon your quality of sleep at night. Eskelinen, M. H., T. Ngandu, et al. (2009). "Midlife Coffee and Tea Drinking and the Risk of Late-Life Dementia: A Population-Based CAIDE Study." *Journal of Alzheimer's Disease* **16**(1): 85-91.

[00478] Diets low in animal fat, such as the Mediterranean-style diet, have been shown to decrease risk of Alzheimer’s disease (*Sofi et al. BMJ 337(sep11_2): a1344- (2008)*)

[00479] D) Prescription Medications

[00480] Statins (such as atorvastatin, brand name Lipitor®) have been shown to decrease the risk of Alzheimer’s disease (*Jick et al. The Lancet 356(9242): 1627-1631 (2000)*)

[00481] E) Over-the-counter Medications

[00482] Taking non-steroidal anti-inflammatory medications (such as Ibuprofen) have been shown to decrease the risk of Alzheimer’s disease (*Vlad, et al. Neurology 70(19): 1672-1677 (2008)*)

[00483] F) Monitoring Modalities

[00484] Brain Scans (such as PIB-PET and FDDNP-) provide indications of disease onset and progression (*Shin et al. "Multitracer PET imaging of amyloid plaques and neurofibrillary tangles in Alzheimer's disease." NeuroImage, In Press, Corrected Proof*)

[00485] Mini-mental exams provided by a healthcare provider can also assess disease onset and progression (*Commenges et al. Epidemiology 3(2): 185-188 (1992)*)

[00486] G) Vitamins, Herbs, or Alternative Treatments

[00487] Omega-3 Fatty Acids, such as those found in fish and also Fish Oil supplements, have been found to decrease the risk of Alzheimer's disease (*Morris et al. Arch Neurol 60(7): 940-946 (2003)*)

[00488] Yoga or meditation to help decrease stress may decrease the risk of Alzheimer's disease (*Kidd. Altern Med Rev. 13(2):85-115 (2008)*)

[00489] H) Associated Diseases or Conditions

[00490] High blood pressure – Lowering blood pressure to the normal range has been shown to reduce the risk of Alzheimer's disease (*Forette et al. Arch Intern Med 162(18): 2046-2052 (2002)*)

[00491] I) Current Treatments

[00492] Medications called "Acetylcholinesterase inhibitors" have been shown to slow the progression of Alzheimer's disease and may help with some symptoms. (*Rogers et al. Neurology 50(1): 136-14 (1998).*). Examples include Donepezil (brand name Aricept®), Rivastigmine (brand name Exelon®), and Galantamine (brand name Reminyl®).

[00493] Medications called "NMDA antagonists" have also been shown to slow progression of Alzheimer's disease and may help with some symptoms. (*Emre et al. Journal of Alzheimer's Disease 14(2): 193-199 (2008)*). Examples include Memantine (Namenda®)

[00494] J) Future Treatments

[00495] A new medication called "PBT2" is currently in clinical testing and data indicates that it may help treat Alzheimer's disease. (*Lannfelt et al. The Lancet Neurology 7(9): 779-786 (2008)*)

[00496] K) Being Connected to a Medical Professional

[00497] Recommendation or referral to see a Neurologist or Preventive Medicine Specialist who may then be able to assess a base-line status and follow the patient as they oversee the preventive medicine recommendations as well as continuing to assess disease development or progression or both.

[00498] Recommendation or referral to see a Nutritionist in order to assess the patient's diet in light of their increased risk for Alzheimer's disease

[00499] L) Common Misconceptions

[00500] Vitamin C supplementation has been shown in numerous studies to not be significantly beneficial in the prevention of Alzheimer's disease. (*Gray, M. L. A. P. K. C. J. C. S. B. W. M. J. D. B. L. T. E. L. Journal of the American Geriatrics Society 56(2): 291-295 (2008); Luchsinger et al. Arch Neurol 60(2): 203-208 (2003)*)

Example 9: Database Construction

[00501] The following example illustrates a database applicable to humans; however, databases for non-human organisms may be constructed or adopted in a similar manner. An example of entries for a deterministic (monogenic / mendelian) phenotype, such as a condition, (to determine carrier status), and a predisposition (polygenic or multifactorial) phenotype, such as a condition (to determine risk), into a database, such as a Predictive Medicine Database, with the various fields filled in, is:

[00502] Deterministic (*Monogenic / Mendelian*) Condition

[00503] Disease = Epidermolysis Bullosa Simplex

[00504] Journal Article = Chan, Y. M., Q. C. Yu, et al. (1993). "The genetic basis of Weber-Cockayne epidermolysis bullosa simplex." Proceedings of the National Academy of Sciences of the United States of America 90(15): 7414-7418.

[00505] Gene Name (from NCBI databases) = Keratin 5

[00506] Gene Symbol(s) (from NCBI databases) = KRT5, K5, CK-5, CK5, DDD, EBS2, KRT5A

[00507] Gene Locus (from NCBI databases) = 12q12-q13

[00508] Exact Genetic Variant Identification (from article, NCBI or Ensemble databases) = I161S

[00509] 50bp downstream of variant (from Ensemble database) =

[00510] TGTCAACCAGAGTCTCCTGACTCCCCCTCAACCTGCAAATCGACCCCAGCA

[00511] 50bp upstream of variant (from Ensemble database) =

[00512] CCAGAGGGTGAGGACCGAGGAGCGCGAGCAGATCAAGACCCTCAACAATA

[00513] IUPAC Nucleotide Code = K

[00514] Exact Position on Chromosome 12 (from Ensemble database, coordinate system) = 51199866

[00515] Strand Direction (from article, NCBI or Ensemble databases) = Reverse

[00516] Location in Gene (from article, NCBI or Ensemble databases) = Exon

[00517] Amino Acid Position (from article, NCBI or Ensemble databases) = 161

[00518] Amino Acid Change (from article, NCBI or Ensemble databases) = Ile→Ser

[00519] Function: Missense

[00520] Allele 1 = T

[00521] Allele 2 = G

[00522] Phenotype-Associated Allele = G

[00523] Genetic Risk Prediction Algorithm Assessment, also referred to as Prediction of Effect of Genetic Variant Algorithm Value - FANS: Risk Level = High; Risk Type = Mis-sense (Non-Conservative Change)

[00524] Inheritance = Autosomal Dominant (AD)

[00525] Replication Status = Monogenic / Replicated

[00526] GVP Rank = Mono (Monogenic genetic variants are assigned a GVP Rank = Mono)

[00527] Genetic Variant-Disease Coefficient (GVDC, also referred to as GVP Score) = 2

[00528] Genetic Variant-Phenotype Clinical Significance Rating (CSR, also referred to as GVP Triage) = 2

[00529] Study Type = Case Study

[00530] Journal Article Author's Name = Chan et. al.

[00531] Date of Publication = 1993

[00532] Name of Journal = Proceedings of the National Academy of Sciences of the United States of America

[00533] Primary Reference = Chan, Y. M., Q. C. Yu, et al. (1993). "The genetic basis of Weber-Cockayne epidermolysis bullosa simplex." Proceedings of the National Academy of Sciences of the United States of America 90(15): 7414-7418.

[00534] Other Reference(s) = Ehrlich, P., V. P. Sybert, et al. (1995). "A Common Keratin 5 Gene Mutation in Epidermolysis Bullosa Simplex-Weber-Cockayne." J Investig Dermatol 104(5): 877-879.

[00535] Predisposition *or Risk (Polygenic or Multifactorial) Condition*

[00536] Disease = Inflammatory Bowel Disease

[00537] Journal Article = Labbe, C., P. Goyette, et al. (2008). "MAST3: a novel IBD risk factor that modulates TLR4 signaling." Genes Immun. 9(7): 602-12.

[00538] Gene Name (from NCBI databases) = Microtubule associated serine/threonine kinase 3

[00539] Gene Symbol(s) (from NCBI databases) = MAST3, KIAA0561

[00540] Gene Locus (from NCBI databases) = 19p13.11

[00541] Exact Genetic Variant Identification (from article or NCBI databases or both) = rs8108738

[00542] Location in Gene = Exon

[00543] Amino Acid Position = 861

[00544] Amino Acid Change = Ser → Gly

[00545] Strand Direction (from article or NCBI databases) = Forward

[00546] Function = Missense

[00547] Allele 1 = A

[00548] Allele 2 = G

[00549] Phenotype-associated Allele = G

[00550] Genetic Risk Prediction Algorithm Assessment, also referred to as Prediction of Effect of Genetic Variant Algorithm Value - PupaSuite: NON_SYNONYMOUS_CODING; ESE: sc35, ENST00000262811, [score: 3.67 (G), new score: 3.22 (A) - Maintain (-0.45)]; ESE: sf2, ENST00000262811, [score: 4.17 (G), new score: 4.62 (A) - Maintain (0.45)]; ESE: sf2, ENST00000262811, [score: 2.23 (G), new score: 1.30 (A) - Lose (-0.93)]; MutDB: Not found within database; FastSNP: Risk level = Low-Medium (2-3); Missense (conservative); Splicing regulation; SNPs3D: SVM Profile = 1.13; VisualSNP: Risk Level = Medium; Mis-sense (Splicing Regulation)

[00551] Risk Value = 1.19

[00552] Risk Type = OR

[00553] Risk Value Confidence Interval = 1.05-1.34

[00554] Risk Value p-value = 0.002

[00555] Cumulative or Absolute Risk or Other Value = Not stated

[00556] MAF = 0.468

[00557] Specific Population(s) = Italian, Canadian, United States

[00558] Incidence of non-phenotype associated allele in disease cohort = Data not supplied

[00559] Incidence of phenotype-associated allele in control cohort = Data not supplied

[00560] Total number in disease cohort = 1105

[00561] Inheritance = Not stated

[00562] Replication Status = Not Replicated

[00563] Genetic Variant-Disease Coefficient (also referred to as GVP Score) = 1

[00564] Genetic Variant-Phenotype Clinical Significant Rating (CSR, also referred to as GVP Triage) = 2

[00565] SNP Rank = 1

[00566] Study Type = Combined Association Mapping Study & Case-Control Study

[00567] Journal Article Author's Name = Labbe et al.

[00568] Date of Publication = 2008

[00569] Name of Journal = Genes and Immunity

[00570] Primary Reference = Labbe, C., P. Goyette, et al. (2008). "MAST3: a novel IBD risk factor that modulates TLR4 signaling." Genes Immun. 9(7): 602-12.

[00571] Other References = None

Example 10 (prophetic): Use of the Methods of the Present Disclosure to Improve, Rescue and/or Resurrect Clinical Trials

[00572] The following example describes use of the methods of the present disclosure to improve or resurrect clinical trials and illustrates methodologies and uses applicable to humans. However, similar methodologies and uses can also be applied or adopted to non-human organisms. A medication in phase II human clinical trials is associated with an adverse drug event in 10% of the study participants, such as neutropenia. Since the exact cause of the neutropenia can not be ascertained, the pharmaceutical company conducting the trial is be unable to determine who is at risk for neutropenia and who is not. With the use of a panel of phenotypes, this additional genetic data is able to be correlated (by regression analysis or other bioinformatic or statistical analysis) with a specific pattern of one or more genetic variants. A research and clinical trial panel may include hundreds of genes that contain genetic variants of clinical significance and the panel acts as a screen, so that instead of knowing exactly what gene or genetic variant to test for, instead many different genes are tested for and/or analyzed all at once, thereby allowing the results to identify any genetic variants that are correlated with the phenotype of interest (such as an adverse drug event) and therefore the results do not require a preconceived notion regarding what genetic variant or what correlation to test.

[00573] It is found that a statistically significant number of participants who have the adverse drug event carry a genetic variant in their CFTR gene on chromosome 7. This genetic variant is associated with cystic fibrosis or congenital bilateral absence of the vas deferens when it exists in trans with another CFTR disease-associated genetic variant. However genetic testing and/or analysis shows that when exposed to the specific medication being tested in this clinical trial, organisms who ‘carry’ this specific genetic variant, meaning they may not have any observable clinical phenotype because they just carry the genetic variant and are not affected by a phenotype, are actually the organisms who have a much higher incidence of neutropenia, possible because of slight molecular changes to the chloride channels in their cells, due to this CFTR genetic variant. Therefore, there now exists a way to differentiate who will have this severe adverse event to the medication and who will not (by conducting genetic testing and/or analysis for this specific genetic variant) and this augments the chances of eventual FDA and/or EU approval, thereby ‘rescuing’ the clinical trial from possible failure.

Example 11 (prophetic): Alternative Use of the Methods of the Present Invention to Improve, Rescue and/or Resurrect Clinical Trials

[00574] The following example illustrates alternative uses of the methods disclosed herein to improve, rescue and/or resurrect clinical Trials. Such alternative uses may also be applicable or adopted to scenarios involving non-human organisms. In this example, a medication under development by a biotech-pharma company is found to have no response in a segment of the population being studied in their research. It is found that 40% of organisms show no response, while the other 60% show a very favorable response to the medication in the treatment of their disease. The Research & Clinical Trial Panel (FIG. 141) is run on all study participants and the genetic testing and analysis, including bioinformatic and regression analysis, shows that the non-responders have a common genetic variation’s genotype in their CYP2D6 gene on chromosome 22 along with two other genetic variations, a genetic variant’s genotype in their TPMT gene on chromosome 6 and a genetic variant’s genotype in their UGT1A1 gene on chromosome 2. All three of these genetic variant’s and their genotypes for a specific genetic profile are able to discern between responders and non-responders. Further research confirms that this specific genetic profile’s association with the non-responder phenotype is statistically significant and can be utilized to segment the population according to responder and non-responder based on this medication under investigation. Further research shows that the non-responders actually has a beneficial response if the starting dose of the medication is tripled and now this same genetic profile can be utilized to determine appropriate starting dose in order to augment chances of appropriate response.

Example 12 (prophetic): Use of the Methods of the Present Invention to Evaluate Individuals for Phenotypes Relevant to Living in Close Quarters

[00575] The following example illustrates use of the methods disclosed herein to evaluate individuals for phenotypes relevant to living in close quarters. Although this example applies to

humans; similar uses can be applied or adopted to evaluate non-human organisms. Infectious diseases are highly communicable and spread extremely fast when organisms live in close quarters, such as military barracks, dormitories, assisted living centers, skilled nursing facility, or retirement home or community. Psychiatric illness and other phenotypes can also have profound effect and cause severe disruption or even increased morbidity or mortality for the subject or for other occupants in these living situations. The Close Living Quarters Panel allows for genetic testing and/or genetic analysis of the phenotypes that may want to be taken into consideration by either an occupant of one of these places, or by a health care professional or a housing administrator or housing official. The methods of the present invention are used to test and analyze organisms living in a military barracks for genetic variants related to the phenotypes related to diseases, disorders, conditions relevant to, or arising from, close living quarters. The results identify organisms who are at much greater risk of meningitis, as well as death from meningitis, and therefore these organisms are singled out and given prophylactic therapy whenever there is a case or suspected case of meningitis at or near where these organisms live.

Example 13 (prophetic): Use of the Methods of the Present Invention for Analysis of Biological Samples

[00576] The following example illustrates use of the methods disclosed herein for analysis of biological samples. Although this example applies to humans; similar uses can be applied or adopted to analyze biological samples of non-human organisms. Pathologists, medical examiners, researchers, corporations, police, military, and other entities store and utilize a large number of biological samples from animals and humans so that those biological samples can be studied then or at some time in the future. A pathology and tissue repository panel is run on either the organism who submits the biological sample or on the biological sample itself. This panel allows for the rapid identification of the biological sample as well as creating a genetic profile of the sample at clinically-relevant genetic variants throughout the genome. This profile (or one or more genetic variant's alleles or genotypes) is stored electronically or on paper, such as in a database, and this database is then be searched to identify tissue (biological samples) that has a specific genetic profile (one or more specific genetic variant's allele or genotypes) so that those tissue samples can then be accessed and utilized. The panel looks at a large number of clinically relevant genetic variants, including all pharmacogenomic-related genetic variants, cancer-related genetic variants, and heart-disease related genetic variants. The panel also assesses the lineage, ancestry, gender and ethnicity of the biological sample so that if that information is not present, it can be ascertained through the use of this panel.

Example 14 (prophetic): Reflex Testing

[00577] Using the methods of genetic testing and analysis described herein, an organism is found to be at increased risk for the initial phenotype of myocardial infarction. Reflex testing is then performed for phenotypes that are useful for evaluating the effectiveness of antiplatelet medications (such as acetylsalicylic acid and/or thienopyridines, such as Clopidogrel); the effectiveness of anti-

thrombotic medications; the appropriate dosing of anti-thrombotics (such as warfarin); the effectiveness of lipid-lowering medications (e.g., statins); the risk of adverse events with lipid-lowering medications, antiplatelets, and/or anti-thrombotic medications; the risk of depression and/or suicidality due to stress and/or serious illness; modification of risk of myocardial infarction with the consumption of specific foods, caffeine and/or alcohol; the risk of cognitive decline after coronary artery bypass graft surgery; and the risk (and/or carrier status) of sudden death due to cardiac arrhythmias. Results indicating that the organism is at increased or decreased risk, predisposition, or carrier status of a reflex (second round) phenotype, in-turn, triggers further reflex testing. If an increased risk for depression is found then this reflexes to a genetic test and/or genetic analysis of the organism's risk, predisposition, or carrier status for phenotypes relating to the effectiveness and/or dosing of medications used to treat depression (such as selective serotonin reuptake inhibitors). If an increased risk of cardiac arrhythmias is found for the organism then this reflexes to genetic analysis of and/or testing for the organism's risk, predisposition, or carrier status for phenotypes indicating the effectiveness, choice, and/or dose of anti-arrhythmogenic medication; the risk (and/or carrier status) of drug Induced Torsade de Pointes; and the risk (and/or carrier status) of the organism for drug induced long QT syndrome.

Table 14: List of Panels- Integrated

<u>List of Panels</u>	<u>List of Panels continued</u>	<u>List of Panels continued</u>
Cat Panel	Dog Panel	Pig Panel
Cat Full Genome Panel	Dog Full Genome Panel	Pig Full Genome Panel
Cat Identification & Tracking Panel	Dog Identification & Tracking Panel	Pig Identificaiton & Tracking Panel
Cat Morphology Panel	Dog Morphology Panel	Pig Lifecycle & Economic Productivity Panel
Cat Allergy Panel	Dog Allergy Panel	Pig Morphology Panel
Cat Conformation Events Panel	Dog Racing Panel	Pig Meat Panel
Cat Companion Panel	Dog Conformation Events Panel	Pig Disease Panel
Cat Learning & Intelligence Panel	Dog Companion Panel	Pig Immune System Panel
Cat Disease Panel	Dog Temperament Panel	Pig Reproduction Panel
Cat Immune System Panel	Dog Learning & Intelligence Panel	Pig Research & Clinical Trial Panel
Cat Longevity Panel	Dog Law Enforcement Panel	Pig Cloning Panel
Cat Research & Clinical Study Panel	Dog Immune System Panel	
Cat Reproduction Panel	Dog Longevity Panel	Sheep Panel
Cat Cloning Panel	Dog Disease Panel	Sheep Full Genome Panel
	Dog Herding and Hunting Panel	Sheep Identification & Tracking Panel
Cattle Panel	Dog Research & Clinical Study Panel	Sheep Lifecycle & Economic Productivity Panel
Cattle Full Genome Panel	Dog Reproduction Panel	Sheep Morphology Panel
Cattle Identification & Tracking Panel	Dog Cloning Panel	Sheep Wool Panel
Cattle Lifecycle & Economic Productivity Panel		Sheep Disease Panel
Cattle Morphology Panel	Goat Panel	Sheep Immune System Panel
Cattle Dairy Panel	Goat Full Genome Panel	Sheep Reproduction Panel
Cattle Meat Panel	Goat Identification & Tracking Panel	Sheep Cloning Panel
Cattle Disease Panel	Goat Lifecycle & Economic Productivity Panel	
Cattle Immune System Panel	Goat Morphology Panel	Turkey Panel
Cattle Growth Panel	Goat Milk Panel	Turkey Full Genome Panel

<u>List of Panels</u>	<u>List of Panels continued</u>	<u>List of Panels continued</u>
Cattle Reproduction Panel	Goat Meat Panel	Turkey Identification & Tracking Panel
Cattle Cloning Panel	Goat Disease Panel	Turkey Lifecycle & Economic Productivity Panel
	Goat Immune System Panel	Turkey Morphology Panel
Chicken Panel	Goat Reproduction Panel	Turkey Meat Panel
Chicken Full Genome Panel	Goat Cloning Panel	Turkey Disease Panel
Chicken Identification & Tracking Panel		Turkey Immune System Panel
Chicken Lifecycle & Economic Productivity Panel	Horse Panel	Turkey Reproduction Panel
Chicken Morphology Panel	Horse Full Genome Panel	Turkey Cloning Panel
Chicken Egg Panel	Horse Identification & Tracking Panel	
Chicken Growth Panel	Horse Lifecycle & Economic Productivity Panel	Rat Panel
Chicken Disease Panel	Horse Morphology Panel	Rat Full Genome Panel
Chicken Immune System Panel	Horse Racing Panel	Rat Identification & Tracking Panel
Chicken Reproduction Panel	Horse Sports Panel	Rat Lifecycle Panel
Chicken Cloning Panel	Horse Disease Panel	Rat Morphology Panel
	Horse Immune System Panel	Rat Pharmacogenomics Panel
Chimpanzee Panel	Horse Worker Panel	Rat Disease Panel
Chimpanzee Full Genome Panel	Horse Reproduction Panel	Rat Cancer Panel
Chimpanzee Identification & Tracking Panel	Horse Cloning Panel	Rat Immune System Panel
Chimpanzee Lifecycle Panel		Rat Reproduction Panel
Chimpanzee Morphology Panel	Mouse Panel	Rat Research & Clinical Trial Panel
Chimpanzee Learning & Intelligence Panel	Mouse Full Genome Panel	Rat Cloning Panel
Chimpanzee Pharmacogenomics Panel	Mouse Identification & Tracking Panel	
Chimpanzee Research & Clinical Trial Panel	Mouse Lifecycle Panel	Custom Panel Option
Chimpanzee Disease Panel	Mouse Morphology Panel	Specific Breed or Strain Option
Chimpanzee Cancer Panel	Mouse Pharmacogenomics Panel	Transgenics Option
Chimpanzee Immune System Panel	Mouse Disease Panel	OP-CADI Option
Chimpanzee Reproduction Panel	Mouse Cancer Panel	Only Decreased Risk Option
Chimpanzee Cloning Panel	Mouse Immune System Panel	Only Increased Risk Option

<u>List of Panels</u>	<u>List of Panels continued</u>	<u>List of Panels continued</u>
	Mouse Reproduction Panel	Specific Phenotype Exclusion Option
Unknown Organism Identification Panel	Mouse Research & Clinical Trial Panel	Universal Identifier Option
Organism Threat Assessment Panel	Mouse Cloning Panel	

[00578] While preferred embodiments of the present invention have been shown and described herein, it will be obvious to those skilled in the art that such embodiments are provided by way of example only. Numerous variations, changes, and substitutions will now occur to those skilled in the art without departing from the invention. It should be understood that various alternatives to the embodiments of the invention described herein may be employed in practicing the invention. It is intended that the following claims define the scope of the invention and that methods and structures within the scope of these claims and their equivalents be covered thereby.

What is claimed is:

Claim 1. A method of predicting a genetic predisposition or carrier status of a potential non-human offspring comprising:

a) identifying one or more genetic variants in the genome of the potential mother of a potential offspring, or obtaining one or more previously-identified genetic variants in the genome of the potential mother, wherein each of the genetic variants is associated with a phenotype;

b) identifying one or more genetic variants in the genome of the potential father of a potential offspring, or obtaining one or more previously-identified genetic variants in the genome of the potential father, wherein each of the genetic variants is associated with a phenotype;

c) calculating the predisposition or carrier status of the potential offspring's mother for the phenotype wherein the predisposition or carrier status is based on the set of genetic variants;

d) calculating the predisposition or carrier status of the potential offspring's father for the phenotype wherein the predisposition or carrier status is based on the set of genetic variants;

e) calculating the potential offspring's predisposition or carrier status for the phenotype wherein the calculating is based on combining the results of step c) and d).

Claim 2. The method of claim 1, further comprising repeating steps a) through e), wherein the potential mother is different from the potential mother of step a), or wherein the potential father is different from the potential father of step b).

Claim 3. The method of claim 2, comprising repeating steps a) through e), with a plurality of potential mothers or a plurality of potential fathers and combining the results to predict the probability of a genetic predisposition or carrier status of a potential offspring from a population of potential mothers or fathers.

Claim 4. The method of claim 2, further comprising selecting a potential father or potential mother for breeding based on the potential offspring with the highest risk or predisposition for a phenotype or the Claim lowest risk or predisposition for a phenotype.

Claim 5. The method of claim 1, wherein the genetic variants of steps a) and b) comprise:

variants located on an autosomal chromosome, a non-autosomal chromosome, a mitochondrial chromosome, a cytoplasmic chromosome, a plasmid chromosome, or a chloroplast chromosome.

Claim 6. The method of claim 1, wherein the potential offspring, potential father or potential mother:

is a dog, a chicken, a cow, a cat, a pig, a horse, a sheep, a fish or a plant;

will be born and live on a country farm, a city farm, a farm with less than 100 animals, a farm with more than 100 animals, a farm with more than 1,000 animals, a farm with more than 10,000 animals, an urban household with children, an urban household without children, a fishery, a stable, a mill, a ranch, a field, a greenhouse, a valley, a mountain, or a free-range; or

is a companion to humans, work-related, production-related, transgenic related, food-related, environment-related or aesthetic-related organism.

Claim 7. The method of claim 1, wherein at least one of said phenotypes:

is a rare disease;

follows a monogenic inheritance;

follows a multifactorial inheritance;

follows a polygenic inheritance; or

is listed in the following figures: General Cattle Panel (15A to 15D); Cattle Dairy Panel (15D to 15G); Cattle Disease Panel (15H); Cattle Growth Panel (15H to 15I); Cattle Lifecycle; Economic Productivity Panel (15I to 15L); and Cattle Meat Panel (15M to 15BB) General Chicken Panel (16A to 16B); Chicken Disease Panel (16B to 16C); Chicken Egg Panel (16C); Chicken Growth Panel (16C to 16D); Chicken Immune System Panel (16D);); Chicken Lifecycle and Economic Productivity Panel (16D to 16F); Chicken Morphology Panel (16F to 16G); Chicken Reproduction Panel (16G to 16H); General Dog Panel (17A); Companion Panel (17A to 17C); Dog Conformation Events Panel (17C to 17D); Dog Disease Panel (17D to 17E); Dog Herding and Hunting Panel (17E); Dog Law Enforcement Panel (17E to 17F); Dog Learning and Intelligence Panel (17F); Dog Morphology Panel (17F to 17G); Dog Racing Panel (17G); Dog Research & Clinical Study Panel (17G to 17J); General Horse Panel (18A); Horse Lifecycle and Economic Productivity Panel (18A-18B); Horse Morphology Panel (18B); Horse Racing/Sports Panel (18B); Horse Reproduction Panel (18B); Horse Worker Panel (18C); General Pig Panel (19A to 19C); Pig Meat Panel (19C to 19D); Pig Morphology Panel (19D to 19E); Pig Reproduction Panel (19E); Pig Disease Panel (19E to 19F); Pig Lifecycle and Economic Productivity Panel (19F to 19H) or a general panel relevant to sheep (20).

Claim 8. The method of claim 1, further comprising reporting a genetic predisposition or carrier status of a potential offspring.

Claim 9. The method of claim 8, wherein reporting said genetic predisposition or carrier status of a potential offspring comprises:

reporting to a company that owns the potential mother or father, an individual who owns the potential mother or father, a company or individual that would own the potential offspring or a third party;

reporting by e-mail, a website, paper, a telephone call, on a CD-ROM, on an electronic storage device, a text message, transmission over a network, or in person; or

providing a pedigree analysis.

Claim 10. The method of claim 1, further comprising providing a medical recommendation or treatment based on the organ system score.

Claim 11. The method of claim 10, wherein said medical recommendation or treatment is provided by a veterinarian, biologist, physician, artificial insemination specialist, anesthesiologist, bacteriologist, cattle specialist, cat specialist, cardiologist, chicken specialist, cloning specialist, dermatologist, dog specialist, endocrinologist, gastroenterologist, geneticist, goat specialist, governmental agency representative, cultivator, hematologist, horse specialist, infectious disease specialist, immunologist, fertility specialist, mouse specialist, nutrition and obesity specialist, neurologist, obstetrician, gynecologist, oncologist, ophthalmologist, pig specialist, pharmacologist, primate specialist, psychiatrist, pulmonologist, rancher, rat specialist, reproduction specialist, rheumatologist, surgeon, transgenic specialist, urologist, or virologist.

Claim 12. The method of claim 1, wherein said previously identified genetic variants:

comprise at least five genes;

comprise at least two genetic variants, each of which is correlated to the same phenotype;

comprise at least 10 single nucleotide polymorphisms;

comprise at least 50 single nucleotide polymorphisms (SNPs), wherein each SNP is correlated to a phenotype ;

comprise at least one variant listed in figures 15-23; or

comprise at least one variant listed in the following figures: General Cattle Panel (15A to 15D); Cattle Dairy Panel (15D to 15G); Cattle Disease Panel (15H); Cattle Growth Panel (15H to 15I); Cattle Lifecycle; Economic Productivity Panel (15I to 15L); and Cattle Meat Panel (15M to 15BB) General Chicken Panel (16A to 16B); Chicken Disease Panel (16B to 16C); Chicken Egg Panel (16C); Chicken Growth Panel (16C to 16D); Chicken Immune System Panel (16D);); Chicken Lifecycle and Economic Productivity Panel (16D to 16F); Chicken Morphology Panel (16F to 16G); Chicken Reproduction Panel (16G to 16H); General Dog Panel (17A); Companion Panel (17A to 17C); Dog Conformation Events Panel (17C to 17D); Dog Disease Panel (17D to 17E); Dog Herding and Hunting Panel (17E); Dog Law Enforcement Panel (17E to 17F); Dog Learning and Intelligence Panel (17F); Dog Morphology Panel (17F to 17G); Dog Racing Panel (17G); Dog Research & Clinical Study Panel (17G to 17J); General Horse Panel (18A); Horse Lifecycle and Economic Productivity Panel (18A-18B); Horse Morphology Panel (18B); Horse Racing/Sports Panel (18B);

Horse Reproduction Panel (18B); Horse Worker Panel (18C); General Pig Panel (19A to 19C); Pig Meat Panel (19C to 19D); Pig Morphology Panel (19D to 19E); Pig Reproduction Panel (19E); Pig Disease Panel (19E to 19F); Pig Lifecycle and Economic Productivity Panel (19F to 19H) or a general panel relevant to sheep (20).

Claim 13. The method of claim 0.1, wherein calculating the potential offspring's predisposition or carrier status for a phenotype further comprises calculating the predisposition or carrier status based on gender, breed, strain, age, weight or purpose of the potential mother or potential father.

Claim 14. A method of determining an organ system score for a non-human organism comprising:

- a) identifying a set of genetic variants in an organism, wherein said genetic variants relate to an organ system phenotype;
- b) calculating the predisposition or carrier status of said organism for at least two phenotypes wherein said predisposition or carrier status is based on said set of genetic variants;
- c) combining the results of steps a) and b) to obtain an organ system score; and
- d) reporting said organ system score.

Claim 15. The method of claim 14, wherein the organ system score is for an organ system selected from the group consisting of: cardiovascular; heart; lung; dermatology; development and learning; ear, nose, and throat; dental; endocrinology; pancreas; thyroid; gastroenterology; hepatology; liver; gall bladder; gynecology; hematology and oncology; immunology; allergy; lactation system, central nervous system, psychological system including but not limited to temperament, infectious diseases; metabolic diseases; rare diseases; male health; musculoskeletal; neonatology; neurology; obstetrics; ophthalmology; pharmacology, toxicology; anesthesiology; psychiatry; reproductive health, rheumatology; sexuality; fertility; sleep medicine; surgery; syndromes; temperament, laryngology; traits and special abilities; obstetrics, otology; urology and nephrology; and vascular; geriatric health; and female health.

Claim 16. The method of claim 14, wherein the organism:

- is a dog, a chicken, a cow, a cat, a pig, a horse, a sheep, a fish or a plant;
- will be born and live on a country farm, a city farm, a farm with less than 100 animals, a farm with more than 100 animals, a farm with more than 1,000 animals, a farm with more than 10,000 animals, an urban household with children, an urban household without children, a fishery, a stable, a mill, a ranch, a field, a greenhouse, a valley, a mountain, or a free-range; or
- is a companion to humans, work-related, production-related, transgenic related, food-related, environment-related or aesthetic-related organism.

Claim 17. The method of claim 14, wherein reporting said organ system score comprises dividing the report into two or more phenotypes.

Claim 18. The method of claim 14, wherein at least one of said at least two phenotypes:

is a rare disease;

follows a monogenic inheritance;

follows a multifactorial inheritance;

follows a polygenic inheritance

is listed in figures 15-23; or

is listed in the following figures: General Cattle Panel (15A to 15D); Cattle Dairy Panel (15D to 15G); Cattle Disease Panel (15H); Cattle Growth Panel (15H to 15I); Cattle Lifecycle; Economic Productivity Panel (15I to 15L); and Cattle Meat Panel (15M to 15BB) General Chicken Panel (16A to 16B); Chicken Disease Panel (16B to 16C); Chicken Egg Panel (16C); Chicken Growth Panel (16C to 16D); Chicken Immune System Panel (16D);); Chicken Lifecycle and Economic Productivity Panel (16D to 16F); Chicken Morphology Panel (16F to 16G); Chicken Reproduction Panel (16G to 16H); General Dog Panel (17A); Companion Panel (17A to 17C); Dog Conformation Events Panel (17C to 17D); Dog Disease Panel (17D to 17E); Dog Herding and Hunting Panel (17E); Dog Law Enforcement Panel (17E to 17F); Dog Learning and Intelligence Panel (17F); Dog Morphology Panel (17F to 17G); Dog Racing Panel (17G); Dog Research & Clinical Study Panel (17G to 17J); General Horse Panel (18A); Horse Lifecycle and Economic Productivity Panel (18A-18B); Horse Morphology Panel (18B); Horse Racing/Sports Panel (18B); Horse Reproduction Panel (18B); Horse Worker Panel (18C); General Pig Panel (19A to 19C); Pig Meat Panel (19C to 19D); Pig Morphology Panel (19D to 19E); Pig Reproduction Panel (19E); Pig Disease Panel (19E to 19F); Pig Lifecycle and Economic Productivity Panel (19F to 19H) or a general panel relevant to sheep (20).

Claim 19. The method of claim 14, wherein reporting said organ system score comprises:

reporting to a company that owns the organism, an individuals who owns the organism or a third party;

reporting by e-mail, a website, paper, a telephone call, on a CD-ROM, on an electronic storage device, a text message, transmission over a network, or in person;

reporting with-in one week of obtaining the organ system score;

reporting the organ system score only when a decreased predisposition to a phenotype is determined; or

reporting the organ system score only when an increased predisposition to a phenotype is determined.

Claim 20. The method of claim 14, wherein reporting said organ system score comprises providing a pedigree analysis.

Claim 21. The method of claim 14, further comprising providing a medical recommendation or treatment based on the organ system score.

Claim 22. The method of claim 21, wherein said medical recommendation or treatment is provided by a veterinarian, biologist, physician, artificial insemination specialist, anesthesiologist, bacteriologist, cattle specialist, cat specialist, cardiologist, chicken specialist, cloning specialist, dermatologist, dog specialist, endocrinologist, gastroenterologist, geneticist, goat specialist, governmental agency representative, cultivator, hematologist, horse specialist, infectious disease specialist, immunologist, fertility specialist, mouse specialist, nutrition and obesity specialist, neurologist, obstetrician, gynecologist, oncologist, ophthalmologist, pig specialist, pharmacologist, primate specialist, psychiatrist, pulmonologist, rancher, rat specialist, reproduction specialist, rheumatologist, surgeon, transgenic specialist, urologist, or virologist.

Claim 23. The method of claim 14, wherein said set of genetic variants:

comprise at least five genes;

comprise at least two genetic variants, each of which is correlated to the same phenotype;

comprise at least 10 single nucleotide polymorphisms;

comprise at least 50 single nucleotide polymorphisms (SNPs), wherein each SNP is correlated to a phenotype

comprise at least one variant listed in figures 15-23; or

comprise at least one variant listed in the following figures: General Cattle Panel (15A to 15D); Cattle Dairy Panel (15D to 15G); Cattle Disease Panel (15H); Cattle Growth Panel (15H to 15I); Cattle Lifecycle; Economic Productivity Panel (15I to 15L); and Cattle Meat Panel (15M to 15BB) General Chicken Panel (16A to 16B); Chicken Disease Panel (16B to 16C); Chicken Egg Panel (16C); Chicken Growth Panel (16C to 16D); Chicken Immune System Panel (16D);); Chicken Lifecycle and Economic Productivity Panel (16D to 16F); Chicken Morphology Panel (16F to 16G); Chicken Reproduction Panel (16G to 16H); General Dog Panel (17A); Companion Panel (17A to 17C); Dog Conformation Events Panel (17C to 17D); Dog Disease Panel (17D to 17E); Dog Herding and Hunting Panel (17E); Dog Law Enforcement Panel (17E to 17F); Dog Learning and Intelligence Panel (17F); Dog Morphology Panel (17F to 17G); Dog Racing Panel (17G); Dog Research & Clinical Study Panel (17G to 17J); General Horse Panel (18A); Horse Lifecycle and Economic Productivity Panel (18A-18B); Horse Morphology Panel (18B); Horse Racing/Sports Panel (18B); Horse Reproduction Panel (18B); Horse Worker Panel (18C); General Pig Panel (19A to 19C); Pig Meat Panel (19C to 19D); Pig Morphology Panel (19D to 19E); Pig Reproduction Panel (19E); Pig

Disease Panel (19E to 19F); Pig Lifecycle and Economic Productivity Panel (19F to 19H) or a general panel relevant to sheep (20).

Claim 24. The method of claim 14, wherein said calculating of the predisposition or carrier status of said organism further comprises calculating the predisposition or carrier status based on gender, breed, strain, age, weight or purpose of the organism.

Claim 25. A method of determining an overall genetic health score of a non-human organism comprising:

- a) identifying a set of genetic variants in an organism;
- b) calculating two or more organ system scores by calculating the predisposition or carrier status of said organism for at least two phenotypes related to each organ system wherein said predisposition or carrier status is based on said set of genetic variants;
- c) combining said two or more organ system scores to obtain an overall genetic health score; and
- d) reporting said overall genetic health score.

Claim 26. The method of claim 25, wherein the organism:

- is a dog, a chicken, a cow, a cat, a pig, a horse, a sheep, a fish or a plant;
- will be born and live on a country farm, a city farm, a farm with less than 100 animals, a farm with more than 100 animals, a farm with more than 1,000 animals, a farm with more than 10,000 animals, an urban household with children, an urban household without children, a fishery, a stable, a mill, a ranch, a field, a greenhouse, a valley, a mountain, or a free-range; or
- is a companion to humans, work-related, production-related, transgenic related, food-related, environment-related or aesthetic-related organism.

Claim 27. The method of claim 25, wherein said two or more organ system scores are for organ systems selected from the group consisting of: cardiovascular; heart; lung; dermatology; development and learning; ear, nose, and throat; dental; endocrinology; pancreas; thyroid; gastroenterology; hepatology; liver; gall bladder; gynecology; hematology and oncology; immunology; allergy; lactation system, central nervous system, psychological system including but not limited to temperament, infectious diseases; metabolic diseases; rare diseases; male health; musculoskeletal; neonatology; neurology; obstetrics; ophthalmology; pharmacology, toxicology; anesthesiology; psychiatry; reproductive health, rheumatology; sexuality; fertility; sleep medicine; surgery; syndromes; temperament, laryngology; traits and special abilities; obstetrics, otology; urology and nephrology; and vascular; geriatric health; and female health.

Claim 28. The method of claim 25, wherein reporting said overall genetic health score comprises:

reporting to a company that owns the organism, an individuals who owns the organism or a third party;

reporting by e-mail, a website, paper, a telephone call, on a CD-ROM, on an electronic storage device, a text message, transmission over a network, or in person;

reporting with-in one week of obtaining the overall genetic health score;

reporting the organ system score only when a decreased predisposition to a phenotype is determined;

reporting the overall genetic health score only when an increased predisposition to a phenotype is determined; or

providing a pedigree analysis.

Claim 29. The method of claim 25, further comprising providing a medical recommendation or treatment based on the overall genetic health score.

Claim 30. The method of claim 29, wherein said medical recommendation or treatment is provided by a veterinarian, biologist, physician, artificial insemination specialist, anesthesiologist, bacteriologist, cattle specialist, cat specialist, cardiologist, chicken specialist, cloning specialist, dermatologist, dog specialist, endocrinologist, gastroenterologist, geneticist, goat specialist, governmental agency representative, cultivator, hematologist, horse specialist, infectious disease specialist, immunologist, fertility specialist, mouse specialist, nutrition and obesity specialist, neurologist, obstetrician, gynecologist, oncologist, ophthalmologist, pig specialist, pharmacologist, primate specialist, psychiatrist, pulmonologist, rancher, rat specialist, reproduction specialist, rheumatologist, surgeon, transgenic specialist, urologist, or virologist.

Claim 31. The method of claim 25, wherein said set of genetic variants:

comprise at least five genes;

comprise at least two genetic variants, each of which is correlated to the same phenotype;

comprise at least 10 single nucleotide polymorphisms;

comprise at least 50 single nucleotide polymorphisms (SNPs), wherein each SNP is correlated to a phenotype

comprise at least one variant listed in figures 15-23; or

comprise at least one variant listed in the following figures: General Cattle Panel (15A to 15D); Cattle Dairy Panel (15D to 15G); Cattle Disease Panel (15H); Cattle Growth Panel (15H to 15I); Cattle Lifecycle; Economic Productivity Panel (15I to 15L); and Cattle Meat Panel (15M to

15BB) General Chicken Panel (16A to 16B); Chicken Disease Panel (16B to 16C); Chicken Egg Panel (16C); Chicken Growth Panel (16C to 16D); Chicken Immune System Panel (16D);); Chicken Lifecycle and Economic Productivity Panel (16D to 16F); Chicken Morphology Panel (16F to 16G); Chicken Reproduction Panel (16G to 16H); General Dog Panel (17A); Companion Panel (17A to 17C); Dog Conformation Events Panel (17C to 17D); Dog Disease Panel (17D to 17E); Dog Herding and Hunting Panel (17E); Dog Law Enforcement Panel (17E to 17F); Dog Learning and Intelligence Panel (17F); Dog Morphology Panel (17F to 17G); Dog Racing Panel (17G); Dog Research & Clinical Study Panel (17G to 17J); General Horse Panel (18A); Horse Lifecycle and Economic Productivity Panel (18A-18B); Horse Morphology Panel (18B); Horse Racing/Sports Panel (18B); Horse Reproduction Panel (18B); Horse Worker Panel (18C); General Pig Panel (19A to 19C); Pig Meat Panel (19C to 19D); Pig Morphology Panel (19D to 19E); Pig Reproduction Panel (19E); Pig Disease Panel (19E to 19F); Pig Lifecycle and Economic Productivity Panel (19F to 19H) or a general panel relevant to sheep (20).

Claim 32. The method of claim 25, wherein said calculating of the predisposition or carrier status of said organism further comprises calculating the predisposition or carrier status based on gender, breed, strain, age, weight or purpose of the organism.

Claim 33. A method of determining and reporting the predisposition or carrier status of a non-human organism for a reflex phenotype comprising:

a) identifying a set of genetic variants in an organism, wherein each of said genetic variants is correlated with a phenotype;

b) determining the predisposition or carrier status of said organism to an initial phenotype and to a reflex phenotype, wherein said predisposition or carrier status is based on said set of genetic variants; and

c) reporting said predisposition or carrier status to the reflex phenotype, wherein the reporting of the predisposition or carrier status to the reflex phenotype depends on the outcome of said determination of predisposition or carrier status to the initial phenotype.

Claim 34. The method of claim 33, wherein said reflex phenotype is:

reported when said organism has an increased predisposition or carrier status for said initial phenotype;

reported when said organism has a decreased predisposition or carrier status for said initial phenotype;

not reported if the organism has neither a decreased or increased predisposition or carrier status for said initial phenotype;

reported concurrently with said initial phenotype;

reported subsequently to said initial phenotype; or
a disease that is positively correlated with said initial phenotype.

Claim 35 The method of claim 33, wherein the organism:

is a dog, a chicken, a cow, a cat, a pig, a horse, a sheep, a fish or a plant;

will be born and live on a country farm, a city farm, a farm with less than 100 animals, a farm with more than 100 animals, a farm with more than 1,000 animals, a farm with more than 10,000 animals, an urban household with children, an urban household without children, a fishery, a stable, a mill, a ranch, a field, a greenhouse, a valley, a mountain, or a free-range; or

is a companion to humans, work-related, production-related, transgenic related, food-related, environment-related or aesthetic-related organism.

Claim 36. The method of claim 33, wherein said initial phenotype comprises:

a rare disease;

follows a monogenic inheritance;

follows a multifactorial inheritance;

follows a polygenic inheritance

one of the phenotypes listed in figures 15-23; or

one of the phenotypes listed in the following figures: General Cattle Panel (15A to 15D); Cattle Dairy Panel (15D to 15G); Cattle Disease Panel (15H); Cattle Growth Panel (15H to 15I); Cattle Lifecycle; Economic Productivity Panel (15I to 15L); and Cattle Meat Panel (15M to 15BB) General Chicken Panel (16A to 16B); Chicken Disease Panel (16B to 16C); Chicken Egg Panel (16C); Chicken Growth Panel (16C to 16D); Chicken Immune System Panel (16D);); Chicken Lifecycle and Economic Productivity Panel (16D to 16F); Chicken Morphology Panel (16F to 16G); Chicken Reproduction Panel (16G to 16H); General Dog Panel (17A); Companion Panel (17A to 17C); Dog Conformation Events Panel (17C to 17D); Dog Disease Panel (17D to 17E); Dog Herding and Hunting Panel (17E); Dog Law Enforcement Panel (17E to 17F); Dog Learning and Intelligence Panel (17F); Dog Morphology Panel (17F to 17G); Dog Racing Panel (17G); Dog Research & Clinical Study Panel (17G to 17J); General Horse Panel (18A); Horse Lifecycle and Economic Productivity Panel (18A-18B); Horse Morphology Panel (18B); Horse Racing/Sports Panel (18B); Horse Reproduction Panel (18B); Horse Worker Panel (18C); General Pig Panel (19A to 19C); Pig Meat Panel (19C to 19D); Pig Morphology Panel (19D to 19E); Pig Reproduction Panel (19E); Pig Disease Panel (19E to 19F); Pig Lifecycle and Economic Productivity Panel (19F to 19H) or a general panel relevant to sheep (20).

Claim 37. The method of claim 33, wherein reporting of the predisposition or carrier status to the reflex phenotype comprises:

reporting to said organism, to an owner, veterinarian, biologist, breeder, specialist in the field, researcher, government agencies, person in-charge of said organism, or to a third party;

reporting by e-mail, a website, paper, a telephone call, on a CD-ROM, on an electronic storage device, a text message, transmission over a network, or in person; or

providing a pedigree analysis.

Claim 38. The method of claim 33, further comprising providing a medical recommendation or treatment based on the predisposition or carrier status to the reflex phenotype.

Claim 39. The method of claim 38, wherein said medical recommendation or treatment is provided by a veterinarian, biologist, physician, artificial insemination specialist, anesthesiologist, bacteriologist, cattle specialist, cat specialist, cardiologist, chicken specialist, cloning specialist, dermatologist, dog specialist, endocrinologist, gastroenterologist, geneticist, goat specialist, governmental agency representative, cultivator, hematologist, horse specialist, infectious disease specialist, immunologist, fertility specialist, mouse specialist, nutrition and obesity specialist, neurologist, obstetrician, gynecologist, oncologist, ophthalmologist, pig specialist, pharmacologist, primate specialist, psychiatrist, pulmonologist, rancher, rat specialist, reproduction specialist, rheumatologist, surgeon, transgenic specialist, urologist, or virologist.

Claim 40. The method of claim 33, wherein said set of genetic variants:

comprise at least five genes;

comprise at least two genetic variants, each of which is correlated to the same phenotype;

comprise at least 10 single nucleotide polymorphisms;

comprise at least 50 single nucleotide polymorphisms (SNPs), wherein each SNP is correlated to a phenotype

comprise at least one variant listed in figures 15-23; or

comprise at least one variant listed in the following figures: General Cattle Panel (15A to 15D); Cattle Dairy Panel (15D to 15G); Cattle Disease Panel (15H); Cattle Growth Panel (15H to 15I); Cattle Lifecycle; Economic Productivity Panel (15I to 15L); and Cattle Meat Panel (15M to 15BB) General Chicken Panel (16A to 16B); Chicken Disease Panel (16B to 16C); Chicken Egg Panel (16C); Chicken Growth Panel (16C to 16D); Chicken Immune System Panel (16D);); Chicken Lifecycle and Economic Productivity Panel (16D to 16F); Chicken Morphology Panel (16F to 16G); Chicken Reproduction Panel (16G to 16H); General Dog Panel (17A); Companion Panel (17A to 17C); Dog Conformation Events Panel (17C to 17D); Dog Disease Panel (17D to 17E); Dog Herding

and Hunting Panel (17E); Dog Law Enforcement Panel (17E to 17F); Dog Learning and Intelligence Panel (17F); Dog Morphology Panel (17F to 17G); Dog Racing Panel (17G); Dog Research & Clinical Study Panel (17G to 17J); General Horse Panel (18A); Horse Lifecycle and Economic Productivity Panel (18A-18B); Horse Morphology Panel (18B); Horse Racing/Sports Panel (18B); Horse Reproduction Panel (18B); Horse Worker Panel (18C); General Pig Panel (19A to 19C); Pig Meat Panel (19C to 19D); Pig Morphology Panel (19D to 19E); Pig Reproduction Panel (19E); Pig Disease Panel (19E to 19F); Pig Lifecycle and Economic Productivity Panel (19F to 19H) or a general panel relevant to sheep (20).

Claim 41. The method of claim 33, wherein said determining the predisposition or carrier status of said organism to a reflex phenotype comprises calculating a predisposition or carrier status based on gender, breed, strain, age, weight or purpose of the organism.

Claim 42. An array comprising at least 25 oligonucleotide sequences attached to a support, wherein each of said sequences is associated with a genetic variant, and the majority of said genetic variants are linked to at least one citation for a scientific article correlating said genetic variant to a phenotype.

Claim 43. The array of claim 42, wherein the sequences are used to determine an organ system score for an organism.

Claim 44. The array of claim 43, wherein the organ system is selected from the group consisting of: cardiovascular; heart; lung; dermatology; development and learning; ear, nose, and throat; dental; endocrinology; pancreas; thyroid; gastroenterology; hepatology; liver; gall bladder; gynecology; hematology and oncology; immunology; allergy; lactation system, central nervous system, psychological system including but not limited to temperament, infectious diseases; metabolic diseases; rare diseases; male health; musculoskeletal; neonatology; neurology; obstetrics; ophthalmology; pharmacology, toxicology; anesthesiology; psychiatry; reproductive health, rheumatology; sexuality; fertility; sleep medicine; surgery; syndromes; temperament, laryngology; traits and special abilities; obstetrics, otology; urology and nephrology; and vascular; geriatric health; and female health.

Claim 45. The array of claim 42, wherein each of said sequence is linked to at least one recommendation from a veterinarian, trainer, rancher, herder, scientist, biologist, physician, owner, caretaker, other healthcare provider of said organism, a government agency, artificial insemination specialist, anesthesiologist, bacteriologist, cattle specialist, cat specialist, cardiologist, chicken specialist, cloning specialist, dermatologist, dog specialist, endocrinologist, gastroenterologist, geneticist, goat specialist, governmental agency representative, cultivator, hematologist, horse specialist, infectious disease specialist, immunologist, fertility specialist, mouse specialist, nutrition and obesity specialist, neurologist, obstetrician, gynecologist, oncologist, ophthalmologist, pig specialist, pharmacologist, primate specialist, psychiatrist, pulmonologist, rancher, rat specialist,

reproduction specialist, rheumatologist, surgeon, transgenic specialist, urologist, virologist, third party or other qualified person.

Claim 46. The array of claim 42, wherein at least one sequence corresponds to a variant listed in the following figures: General Cattle Panel (15A to 15D); Cattle Dairy Panel (15D to 15G); Cattle Disease Panel (15H); Cattle Growth Panel (15H to 15I); Cattle Lifecycle; Economic Productivity Panel (15I to 15L); and Cattle Meat Panel (15M to 15BB) General Chicken Panel (16A to 16B); Chicken Disease Panel (16B to 16C); Chicken Egg Panel (16C); Chicken Growth Panel (16C to 16D); Chicken Immune System Panel (16D);); Chicken Lifecycle and Economic Productivity Panel (16D to 16F); Chicken Morphology Panel (16F to 16G); Chicken Reproduction Panel (16G to 16H); General Dog Panel (17A); Companion Panel (17A to 17C); Dog Conformation Events Panel (17C to 17D); Dog Disease Panel (17D to 17E); Dog Herding and Hunting Panel (17E); Dog Law Enforcement Panel (17E to 17F); Dog Learning and Intelligence Panel (17F); Dog Morphology Panel (17F to 17G); Dog Racing Panel (17G); Dog Research & Clinical Study Panel (17G to 17J); General Horse Panel (18A); Horse Lifecycle and Economic Productivity Panel (18A-18B); Horse Morphology Panel (18B); Horse Racing/Sports Panel (18B); Horse Reproduction Panel (18B); Horse Worker Panel (18C); General Pig Panel (19A to 19C); Pig Meat Panel (19C to 19D); Pig Morphology Panel (19D to 19E); Pig Reproduction Panel (19E); Pig Disease Panel (19E to 19F); Pig Lifecycle and Economic Productivity Panel (19F to 19H) or a general panel relevant to sheep (20).