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(54) Title: METHODS AND SYSTEMS RELATING TO EPIGENETIC PHENOTYPES

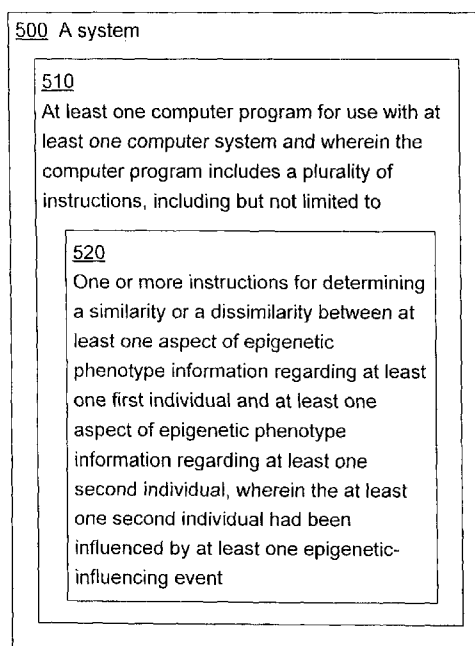


FIG. 5



530

(57) Abstract: In one aspect, a system includes, but is not limited to, at least one computer program for use with at least one computer system and wherein the computer program includes a plurality of instructions, including but not limited to, one or more instructions for determining at least one correlation between at least one epigenetic-influencing event and at least one aspect of epigenetic phenotype information regarding at least one individual.

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Methods and Systems Relating to Epigenetic Phenotypes

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5 CROSS-REFERENCE TO RELATED APPLICATIONS

The present application is related to and claims the benefit of the earliest available effective filing date(s) from the following listed application(s) (the "Related Applications") (e.g., claims earliest available priority dates for other than provisional patent applications or claims benefits under 35 USC § 119(e) for provisional patent applications, for any and all parent, grandparent, great-grandparent, etc. applications of the Related Application(s)).

Related Applications:

For purposes of the USPTO extra-statutory requirements, the present application constitutes a continuation-in-part of United States Patent Application No. 11/880,454 entitled **METHODS AND SYSTEMS RELATING TO EPIGENETIC INFORMATION**, naming Roderick A. Hyde, Muriel Y. Ishikawa, Eric C. Leuthardt, Dennis J. Rivet, and Lowell L. Wood, Jr. as inventors, filed 19 July, 2007, which is currently co-pending, or is an application of which a currently co-pending application is entitled to the benefit of the filing date.

For purposes of the USPTO extra-statutory requirements, the present application constitutes a continuation-in-part of United States Patent Application No. 11/880,453, entitled **METHODS AND SYSTEMS RELATING TO MITOCHONDRIAL DNA INFORMATION**, naming Roderick A. Hyde, Muriel Y. Ishikawa, Eric C. Leuthardt, Dennis J. Rivet, and Lowell L. Wood, Jr. as

inventors, filed **19 July, 2007**, which is currently co-pending, or is an application of which a currently co-pending application is entitled to the benefit of the filing date.

For purposes of the USPTO extra-statutory requirements, the present application constitutes a continuation-in-part of United States Patent Application No.

5 **11/900,050**, entitled **METHODS AND SYSTEMS RELATING TO**

MITOCHONDRIAL DNA PHENOTYPES, naming **Roderick A. Hyde, Muriel Y. Ishikawa, Eric C. Leuthardt, Dennis J. Rivet, and Lowell L. Wood, Jr.** as

inventors, filed **September 7, 2007**, which is currently co-pending, or is an application of which a currently co-pending application is entitled to the benefit of the

10 filing date. The United States Patent Office (USPTO) has published a notice to the

effect that the USPTO's computer programs require that patent applicants reference both a serial number and indicate whether an application is a continuation or

continuation-in-part. Stephen G. Kunin, *Benefit of Prior-Filed Application*, USPTO

Official Gazette March 18, 2003, available at [http://www.uspto.gov/web/offices/com/](http://www.uspto.gov/web/offices/com/sol/og/2003/week11/patbene.htm)

15 [sol/og/2003/week11/patbene.htm](http://www.uspto.gov/web/offices/com/sol/og/2003/week11/patbene.htm). The present Applicant Entity (hereinafter

"Applicant") has provided above a specific reference to the application(s) *from which priority is being claimed* as recited by statute. Applicant understands that the statute

is unambiguous in its specific reference language and does not require either a serial number or any characterization, such as "continuation" or "continuation-in-part," for

20 claiming priority to U.S. patent applications. Notwithstanding the foregoing,

Applicant understands that the USPTO's computer programs have certain data entry requirements, and hence Applicant is designating the present application as a

continuation-in-part of its parent applications as set forth above, but expressly points out that such designations are not to be construed in any way as any type of

25 commentary or admission as to whether or not the present application contains any new matter in addition to the matter of its parent application(s).

All subject matter of the Related Applications and of any and all parent, grandparent, great-grandparent, etc. applications of the Related Applications is

incorporated herein by reference to the extent such subject matter is not inconsistent
30 herewith.

SUMMARY

In one aspect, a method includes, but is not limited to, determining a similarity or a dissimilarity between at least one aspect of epigenetic phenotype information regarding at least one first individual and at least one aspect of epigenetic phenotype information regarding at least one second individual, wherein the at least one second individual had been influenced by at least one epigenetic-influencing event. In addition to the foregoing, other method aspects are described in the claims, drawings, and text forming a part of the present disclosure.

In one or more various aspects, related systems include but are not limited to circuitry or programming for effecting the herein-referenced method aspects; the circuitry or programming can be virtually any combination of hardware, software, or firmware configured to effect the herein-referenced method aspects depending upon the design choices of the system designer.

In one aspect, a system includes, but is not limited to, at least one computer program for use with at least one computer system and wherein the computer program includes a plurality of instructions, including but not limited to, one or more instructions for determining at least one correlation between at least one epigenetic-influencing event and at least one aspect of epigenetic phenotype information regarding at least one individual. In one aspect, a system includes, but is not limited to, at least one computer program for use with at least one computer system and wherein the computer program includes a plurality of instructions, including but not limited to, one or more instructions for determining a similarity or a dissimilarity between at least one aspect of epigenetic phenotype information regarding at least one first individual and at least one aspect of epigenetic phenotype information regarding at least one second individual, wherein the at least one second individual had been influenced by at least one epigenetic-influencing event. In one aspect, a system includes, but is not limited to, at least one computer program for use with at least one computer system and wherein the computer program includes a plurality of instructions, including but not limited to, one or more instructions for determining one or more correlations between at least one aspect of epigenetic phenotype information obtained regarding at least one first individual and information regarding

at least one epigenetic-influencing event in relation to the at least one first individual, and one or more instructions for applying at least one of the one or more correlations to at least one aspect of epigenetic phenotype information regarding at least one second individual. In one aspect, a system includes, but is not limited to, at least one computer program for use with at least one computer system and wherein the computer program includes a plurality of instructions, including but not limited to, one or more instructions for determining one or more correlations between at least one aspect of epigenetic phenotype information obtained regarding at least one first individual and information regarding at least one medical therapy in relation to the at least one first individual, and one or more instructions for applying at least one of the one or more correlations to at least one aspect of epigenetic phenotype information regarding at least one second individual. In one aspect, a system includes, but is not limited to, at least one computer program for use with at least one computer system and wherein the computer program includes a plurality of instructions, including but not limited to, one or more instructions for determining one or more correlations between at least one aspect of epigenetic phenotype information obtained regarding at least one first individual and information regarding at least one environmental event in relation to the at least one first individual, and one or more instructions for applying at least one of the one or more correlations to at least one aspect of epigenetic phenotype information regarding at least one second individual. In addition to the foregoing, other system aspects are described in the claims, drawings, and text forming a part of the present disclosure.

The foregoing summary is illustrative only and is not intended to be in any way limiting. In addition to the illustrative aspects, embodiments, and features described above, further aspects, embodiments, and features will become apparent by reference to the drawings and the following detailed description.

BRIEF DESCRIPTION OF THE FIGURES

FIG. 1 illustrates some aspects of a system that may serve as an illustrative environment for subject matter technologies.

FIG. 2 depicts aspects of a system such as the one illustrated in Fig. 1.

FIG. 3 shows aspects of a system such as the one illustrated in Fig. 1.

FIG. 4 illustrates aspects of a system such as the one illustrated in Fig. 1.

FIG. 5 illustrates some aspects of a system that may serve as an illustrative environment for subject matter technologies.

5 **FIG. 6** depicts aspects of a system such as the one illustrated in Fig. 5.

FIG. 7 shows aspects of a system such as the one illustrated in Fig. 5.

FIG. 8 illustrates aspects of a system such as the one illustrated in Fig. 5.

FIG. 9 shows some aspects of a system that may serve as an illustrative environment for subject matter technologies.

10 **FIG. 10** depicts aspects of a system such as the one illustrated in Fig. 9.

FIG. 11 shows aspects of a system such as the one illustrated in Fig. 9.

FIG. 12 illustrates some aspects of a system that may serve as an illustrative environment for subject matter technologies.

FIG. 13 depicts aspects of a system such as the one illustrated in Fig. 12.

15 **FIG. 14** illustrates some aspects of a system that may serve as an illustrative environment for subject matter technologies.

FIG. 15 shows aspects of a system such as the one illustrated in Fig. 14.

FIG. 16 depicts aspects of a system such as the one illustrated in Fig. 14.

FIG. 17 shows a logic flowchart of a process.

20 **FIG. 18** illustrates a logic flowchart of a process, such as the one shown in Fig. 17.

FIG. 19 depicts a logic flowchart of a process, such as the one shown in Fig. 17.

25 **FIG. 20** shows a logic flowchart of a process, such as the one depicted in Fig. 17.

FIG. 21 shows a logic flowchart of a process.

FIG. 22 illustrates a logic flowchart of a process, such as the one shown in Fig. 21.

30 **FIG. 23** depicts a logic flowchart of a process, such as the one shown in Fig. 21.

FIG. 24 shows a logic flowchart of a process, such as the one depicted in Fig.

21.

FIG. 25 shows a logic flowchart of a process.

FIG. 26 depicts a logic flowchart of a process, such as the one shown in Fig.

5 25.

FIG. 27 shows a logic flowchart of a process.

FIG. 28 illustrates a logic flowchart of a process, such as the one shown in

Fig. 27.

FIG. 29 shows a logic flowchart of a process.

10 FIG. 30 depicts a logic flowchart of a process, such as the one shown in Fig.

29.

DETAILED DESCRIPTION

In the following detailed description, reference is made to the accompanying
15 drawings, which form a part hereof. In the drawings, similar symbols typically
identify similar components, unless context dictates otherwise. The illustrative
embodiments described in the detailed description, drawings, and claims are not
meant to be limiting. Other embodiments may be utilized, and other changes may be
made, without departing from the spirit or scope of the subject matter presented here.

20 This document uses formal outline headings for clarity of presentation.
However, it is to be understood that the outline headings are for presentation
purposes, and that different types of subject matter may be discussed throughout the
application (*e.g.*, device(s)/structure(s) may be described under process(es)/operations
heading(s) or process(es)/operations may be discussed under structure(s)/process(es)
25 headings; or descriptions of single topics may span two or more topic headings).
Hence, the use of the formal outline headings is not intended to be in any way
limiting.

With reference to the figures, and with reference now to Figure 1, depicted is
one aspect of a system that may serve as an illustrative environment of or for subject
30 matter technologies, for example, at least one computer program for use with at least

one computer system and wherein the computer program includes a plurality of instructions, including but not limited to, one or more instructions for determining at least one correlation between at least one epigenetic-influencing event and at least one aspect of epigenetic phenotype information regarding at least one individual.

- 5 Accordingly, first described herein are certain specific example systems of Figure 1; thereafter, there is illustrated certain specific example structures and processes. Those having skill in the art will appreciate that the specific structures and processes described herein are intended as merely illustrative of their more general counterparts.

A. Structure(s) and or System(s)

- 10 Continuing to refer to Figure 1, depicted is a partial view of a system that may serve as an illustrative environment of or for subject matter technologies. One or more users 130 may use a system 100 including at least one computer program 110 for use with at least one computer system, wherein the at least one computer program 110 includes a plurality of instructions. One or more users 130 may include, for
15 example, one or more administrators, medical personnel, pharmacists, geneticists, researchers or technicians. Although a single user is shown in Figure 1, in some embodiments at least one group of users or at least one series of users may interact with the system. In some embodiments, the one or more users 130 may include a computer system, artificial intelligence system (AI) or other circuitry. The at least
20 one computer program 110 may include one or more instructions for determining at least one correlation between at least one epigenetic-influencing event and at least one aspect of epigenetic phenotype information regarding at least one individual 120.

- A correlation may be established by, for example, statistical methods or by a general relationship between the data sets. In some embodiments, the at least one
25 correlation may include at least one statistical correlation. In various aspects, at least one statistical correlation may include, for example, at least one linear correlation, at least one nonlinear correlation, functional dependency or other mathematical relationship. At least one statistical correlation may or may not be associated with some type of causality, real or implied, proven or unproven. At least one statistical
30 correlation may or may not be associated with some type of medical event such as,

for example, illness, allergic reaction, bleeding, stroke, one or more side effects, or death.

For more information regarding epigenetics and epigenetic information, see: Bird, Perceptions of Epigenetics, *Nature* 477, 396-398 (2007); Grewal and Elgin, Transcription and RNA Interference in the Formation of Heterochromatin, *Nature* 447: 399-406 (2007); and Callinan and Feinberg, The Emerging Science of Epigenomics, *Human Molecular Genetics* 15, R95-R101 (2006), each of which are incorporated herein by reference. Epigenetic information may include, for example, information regarding DNA methylation, histone states or modifications, DNA structure, transcriptional activity, RNAi, protein binding or other molecular states. In some embodiments, epigenetic information may include information regarding inflammation-mediated cytosine damage products. See, e.g., Valinluck and Sowers, Inflammation-Mediated Cytosine Damage: A Mechanistic Link Between Inflammation and the Epigenetic Alterations in Human Cancers, *Cancer Research* 67: 5583-5586 (2007), which is incorporated herein by reference.

As used herein, an "epigenetic-influencing event" includes an event that influences the epigenetic phenotype of at least one cell within at least one individual. An epigenetic-influencing event may, but need not, influence every cell in an individual's body, or influence every cell in an organ, region of the body, or tissue. An epigenetic-influencing event may be part of a medical therapy, for example an epigenetic-influencing event may include one or more medications, or one or more treatments. An epigenetic-influencing event may include at least one medical therapy including one or more energy-based procedures, for example radiation therapy, UV therapy, thermal therapy or ultrasound therapy. An epigenetic-influencing event may be noticed at the time of the event, or it may not be noticed by the affected individual or other individuals. An epigenetic-influencing event may include one or more environmental events, such as but not limited to, exposure of an individual to radiation, one or more pollutants, or one or more toxins. An epigenetic-influencing event may happen in a short time interval such as minutes or hours or it may happen over a long time interval such as weeks, months or years. An epigenetic influencing-event may include multiple smaller events, such as multiple small exposures that in

the aggregate influence the epigenetic phenotype of at least one cell within at least one individual. An epigenetic-influencing event may include the personal activities of an individual, including an individual knowingly exposing himself to, for example, toxins. As an example, an epigenetic-influencing event may include the choice of an individual to expose himself to cigarette smoke, or the choice of an individual to work in an environment with a high level of nickel or cadmium. As an example, an epigenetic-influencing event may include the choice of an individual to be in a location where toxins are present, such as in a location where arsenic levels are very high in the drinking water.

As used herein, "epigenetic phenotype information" includes epigenetic phenotype information regarding at least one phenotype of at least one cell. For example, epigenetic phenotype information includes information regarding DNA methylation, histone states or modifications, transcriptional activity, RNAi, protein binding or other molecular states. Epigenetic phenotype information may include temporal information, spatial information, biochemical information, or metabolic information. Epigenetic phenotype information may be stable over time in multiple assays or it may alter over time, for example as cells are renewed, refreshed or replaced. Epigenetic phenotype information may change over time in multiple assays as cells progress through the cell cycle, including through cellular division. The epigenetic phenotype information relating to different cells may be different at a single time point, even when the cells originate from a single individual, including from a single organ or tissue.

Figure 2 depicts alternate embodiments of the system of Figure 1. In some embodiments, the one or more instructions for determining at least one correlation 120 may include at least one of instructions 200, 210, 220, 230 or 240. In some embodiments, the one or more instructions for determining at least one correlation 120 may include embodiments wherein the at least one aspect of epigenetic phenotype information regarding at least one individual comprises at least one aspect of epigenetic phenotype information assayed at more than one time 200. For example, aspects of epigenetic phenotype information may be assayed on multiple occasions or at set intervals, such as weekly or monthly. For example, aspects of

epigenetic phenotype information may be assayed in multiple assays carried out in parallel or in series, and the information from the assays combined into a system. For example, at least one aspect of epigenetic phenotype information may be assayed at irregular intervals, such as when an individual enters into a medical treatment or
5 consults medical personnel. In some embodiments, the one or more instructions for determining at least one correlation 120 may include embodiments wherein the at least one aspect of epigenetic phenotype information regarding at least one individual includes information regarding DNA methylation 210. For example, at least one aspect of epigenetic phenotype information may include information regarding the
10 methylation status of DNA generally or in the aggregate, or information regarding DNA methylation at one or more specific DNA loci, DNA regions, or DNA bases. In some embodiments, the one or more instructions for determining at least one correlation 120 may include embodiments wherein the at least one aspect of epigenetic phenotype information regarding at least one individual includes
15 information regarding histone structure 220. For example, at least one aspect of epigenetic phenotype information may include information regarding histone structure generally or in the aggregate, or histone structure at one or more specific locations including one or more chromosomes. Information regarding histone structure may, for example, include information regarding specific subtypes or classes
20 of histones, such as H1, H2A, H2B, H3 or H4. Information regarding histone structure may be provided by array-based techniques, such as described in Barski et al., High-resolution profiling of histone methylations in the human genome, *Cell* 129, 823-837 (2007), which is incorporated herein by reference. In some embodiments, the one or more instructions for determining at least one correlation 120 may include
25 embodiments wherein the at least one aspect of epigenetic phenotype information regarding at least one individual includes information regarding multiple genomic loci 230. For example, in some embodiments at least one aspect of epigenetic information may include information regarding multiple genomic loci throughout one or more genomes, multiple genomic loci located on one or more chromosomes or
30 chromosomal arms, or multiple genomic loci located in a specific chromosomal region. Information regarding multiple genomic loci may also include information

regarding different epigenetic effects at different genomic loci. See, for example, The ENCODE Project Consortium, Identification and analysis of functional elements in 1% of the human genome by the ENCODE pilot project, *Nature* 447: 799-816 (2007), which is incorporated herein by reference. For example, in some embodiments the

5 information regarding multiple genomic loci may include information regarding both DNA methylation and histone modifications. See, for example, Berger, The Complex Language of Chromatin Regulation During Transcription, *Nature* 477, 407- 412 (2007), and Greally, Encyclopaedia of Humble DNA, *Nature* 447: 782-783 (2007), which are incorporated herein by reference. In some embodiments, the information

10 regarding multiple genomic loci may include information regarding the predicted stability of the epigenetic status at the multiple genomic loci. See, for example, Dodd et al., Theoretical Analysis of Epigenetic Cell Memory by Nucleosome Modification, *Cell* 129, 813-822 (2007), which is incorporated herein by reference. In some embodiments, the information regarding multiple genomic loci may include

15 information regarding the spatial relationship of the genomic loci within at least one cell. For example, see Fraser and Bickmore, Nuclear Organization of the Genome and the Potential for Gene Regulation, *Nature* 477: 413- 417 (2007), which is incorporated herein by reference. In some embodiments, the information regarding multiple genomic loci may include information regarding binding of one or more

20 proteins to multiple genomic loci. See, for example, Xie et al., Systematic Discovery of Regulatory Motifs in Conserved Regions of the Human Genome, Including Thousands of CTCF Insulator Sites, *PNAS USA* 104: 7145-7150 (2007), which is incorporated herein by reference. In some embodiments, the one or more instructions for determining at least one correlation 120 may include embodiments wherein the at

25 least one aspect of epigenetic phenotype information regarding at least one individual includes information regarding mosaicism of at least one individual 240. The term “mosaicism,” as used herein, denotes, for example, situations where two or more cellular subtypes arise during the lifespan of an organism, situations where two or more cellular subtypes originate with the first cell of an organism and situations

30 where the origin of the cellular subtypes is unclear. The term “mosaicism,” as used herein, may include somatic mosaicism, gonadal mosaicism, or chimerism. For

example, at least one aspect of epigenetic information may include information regarding mosaicism of at least one individual such as the presence or absence of mosaicism, the location of mosaicism, the tissue or tissues involved in the mosaicism, or the proportion of various subtypes of cells in mosaic tissue. For more information
5 on somatic mosaicism and disease, see Youssoufian and Pyeritz, Mechanisms and Consequences of Somatic Mosaicism in Humans, *Nature Reviews Genetics* 3: 748-758 (2002), which is incorporated herein by reference.

Figure 3 depicts alternate embodiments of the system of Figure 1. In some embodiments, the one or more instructions for determining at least one correlation
10 120 may include embodiments wherein at least one aspect of epigenetic phenotype information regarding at least one individual includes information regarding at least one tissue source 300. For example, the information regarding at least one tissue source may include information regarding the origin, storage, pathology, pathological subtype, or handling of the tissue. For example, the information regarding at least
15 one tissue source may include information regarding at least one physical, spatial or relative anatomic source. The information regarding at least one individual includes information regarding at least one tissue source 300 may include information regarding at least one abnormal tissue source 310. For example, the information regarding at least one abnormal tissue source may include information regarding a
20 neoplastic source, a dysplastic source, a diseased source, an infectious source or a cancerous source. For example, at least one aspect of epigenetic information may be associated with cancerous tissues, e.g. Ducasse and Brown, Epigenetic Alterations and Cancer, *Molecular Cancer* 5:60 (2006); and Kagen et al., Towards Clinical Application of Methylated DNA Sequences as Cancer Biomarkers, a Joint NCI's
25 EDNRN and NIST Workshop on Standards, Methods, Assays, Reagents and Tools, *Cancer Research* 67:4545-4549 (2007), which are incorporated herein by reference. Also by way of example, some aspects of epigenetic information may be associated with human disease diagnoses, e.g. Feinberg, Phenotypic Plasticity and the Epigenetics of Human Disease, *Nature* 477: 433-440 (2007), which is incorporated
30 herein by reference. The information regarding at least one individual includes information regarding at least one tissue source 300 may include information

regarding at least one type of tissue 320. For example, information regarding at least one type of tissue may include information regarding at least one clinical diagnosis, at least one pathology report, or at least one surgical report. For example, the information regarding at least one type of tissue may include the origin tissue type, the handling of the tissue, or one or more treatments to the tissue. In some embodiments, the information regarding at least one type of tissue may include cellular developmental stage, lineage, or status. See, for example, Reik, Stability and Flexibility of Epigenetic Gene Regulation in Mammalian Development, *Nature* 447:425- 432 (2007), which is incorporated herein by reference.

Continuing to refer to Figure 3, in some embodiments the one or more instructions for determining at least one correlation 120 may include embodiments wherein the at least one epigenetic-influencing event includes at least one medical therapy. For example, an epigenetic-influencing event may include a medical therapy including one or more medications, or one or more treatments. An epigenetic-influencing event may include at least one medical therapy including one or more energy-based procedures, for example radiation therapy, UV therapy, thermal therapy, phototherapy, or ultrasound therapy. In some embodiments the one or more instructions for determining at least one correlation 120 may include embodiments wherein the at least one epigenetic-influencing event includes at least one environmental event. For example, an environmental event may include exposure of an individual to radiation, one or more pollutants, or one or more toxins. For example, an environmental event may include exposure of an individual to excessive levels of di(2-ethylhexyl)phthalate (DEHP). For example, an environmental event may include exposure of an individual to excessive levels of heavy metals, nickel, lead, cadmium, mercury, or arsenic. In some embodiments, an environmental event may include some element of activity by an individual, such as when an individual goes to or stays in a location with exposures such as those described herein.

Figure 4 depicts further aspects of a system such as that shown in Figure 1. The computer program 110 includes a plurality of instructions and may include one or more instructions for correlating the at least one aspect of epigenetic phenotype information regarding at least one individual with previous epigenetic information

regarding the at least one individual, wherein the previous epigenetic information was ascertained prior to the epigenetic-influencing event 400. In some embodiments, one or more instructions for correlating 400 may include instructions wherein the at least one aspect of epigenetic phenotype information is information regarding a subset of data points of the previous epigenetic information 410. For example, an initial assay or group of assays may yield information regarding a large number of data points, while subsequent smaller assays or groups of assays may yield information regarding a smaller group, or subset of data points. For example, an initial assay may yield a large number of data points that are included in the system, while information from further assays that is incorporated into a system is limited to a subset of data points. Also in reference to Figure 4, the computer program 110 includes a plurality of instructions and may include one or more instructions for suggesting at least one intervention strategy for the at least one first individual in reference to the at least one correlation 420. For example, one or more instructions for suggesting at least one intervention strategy may include one or more instructions for suggesting a course of medication, or a medical treatment. For example, one or more instructions for suggesting at least one intervention strategy may include one or more instructions for suggesting the avoidance of a medication, a medical treatment, location, toxin, or environmental pollutant.

Figure 5 depicts a partial view of a system that may serve as an illustrative environment of or for subject matter technologies. One or more users 530 may use a system 500 including at least one computer program 510 for use with at least one computer system, wherein the at least one computer program 510 includes a plurality of instructions. One or more users 530 may include, for example, one or more administrators, medical personnel, pharmacists, geneticists, researchers or technicians. Although a single user is shown in Figure 5, in some embodiments at least one group of users or at least one series of users may interact with the system. In some embodiments, the one or more users 530 may include a computer system, artificial intelligence system (AI) or other circuitry. The at least one computer program 510 may include one or more instructions for determining a similarity or a dissimilarity between at least one aspect of epigenetic phenotype information

regarding at least one first individual and at least one aspect of epigenetic phenotype information regarding at least one second individual, wherein the at least one second individual had been influenced by at least one epigenetic-influencing event 520.

Figure 6 illustrates further aspects of the system shown in Figure 5. In some embodiments, the one or more instructions for determining a similarity or a dissimilarity 520 may include one or more instructions wherein the at least one aspect of epigenetic phenotype information regarding at least one first individual comprises at least one aspect of epigenetic phenotype information assayed at more than one time 600. For example, aspects of epigenetic phenotype information may be assayed on multiple occasions or set intervals, such as weekly or monthly. For example, aspects of epigenetic phenotype information may be assayed in multiple assays carried out in parallel or in series, and the information from the assays combined into a system. For example, at least one aspect of epigenetic phenotype information may be assayed at irregular intervals, such as when an individual enters into a medical treatment or consults medical personnel. In some embodiments, the one or more instructions for determining a similarity or a dissimilarity 520 may include one or more instructions wherein the at least one aspect of epigenetic phenotype information regarding at least one first individual includes information regarding DNA methylation 610. For example, one or more instructions wherein the at least one aspect of epigenetic phenotype information regarding at least one first individual may include information regarding the methylation status of DNA generally or in the aggregate, or information regarding DNA methylation at one or more specific DNA loci, DNA regions, or DNA bases. In some embodiments, the one or more instructions for determining a similarity or a dissimilarity 520 may include one or more instructions wherein the at least one aspect of epigenetic phenotype information regarding at least one first individual includes information regarding histone structure 620. For example, at least one aspect of epigenetic phenotype information may include information regarding histone structure generally or in the aggregate, or histone structure at one or more specific locations including one or more chromosomes. Information regarding histone structure may, for example, include information regarding specific subtypes or classes of histones, such as H1, H2A, H2B, H3 or H4. Information regarding

histone structure may be provided by array-based techniques, such as described in Barski et al., High-resolution profiling of histone methylations in the human genome, *Cell* 129, 823-837 (2007), which is incorporated herein by reference. In some embodiments, the one or more instructions for determining a similarity or a dissimilarity 520 may include one or more instructions wherein the at least one aspect of epigenetic phenotype information regarding at least one first individual includes information regarding multiple genomic loci 630. For example, in some embodiments at least one aspect of epigenetic information may include information regarding multiple genomic loci throughout one or more genomes, multiple genomic loci located on one or more chromosomes or chromosomal arms, or multiple genomic loci located in a specific chromosomal region. Information regarding multiple genomic loci may also include information regarding different epigenetic effects at different genomic loci. See, for example, The ENCODE Project Consortium, Identification and analysis of functional elements in 1% of the human genome by the ENCODE pilot project, *Nature* 447: 799-816 (2007), which is incorporated herein by reference. For example, in some embodiments the information regarding multiple genomic loci may include information regarding both DNA methylation and histone modifications. See, for example, Berger, The Complex Language of Chromatin Regulation During Transcription, *Nature* 477, 407- 412 (2007), and Greally, Encyclopaedia of Humble DNA, *Nature* 447: 782-783 (2007), which are incorporated herein by reference. In some embodiments, the information regarding multiple genomic loci may include information regarding the predicted stability of the epigenetic status at the multiple genomic loci. See, for example, Dodd et al., Theoretical Analysis of Epigenetic Cell Memory by Nucleosome Modification, *Cell* 129, 813-822 (2007), which is incorporated herein by reference. In some embodiments, the information regarding multiple genomic loci may include information regarding the spatial relationship of the genomic loci within at least one cell. For example, see Fraser and Bickmore, Nuclear Organization of the Genome and the Potential for Gene Regulation, *Nature* 477: 413- 417 (2007), which is incorporated herein by reference. In some embodiments, the information regarding multiple genomic loci may include information regarding binding of one or more

proteins to multiple genomic loci. See, for example, Xie et al., Systematic Discovery of Regulatory Motifs in Conserved Regions of the Human Genome, Including Thousands of CTCF Insulator Sites, *PNAS USA* 104: 7145-7150 (2007), which is incorporated herein by reference. In some embodiments, the one or more instructions

5 for determining a similarity or a dissimilarity 520 may include one or more instructions wherein the at least one aspect of epigenetic phenotype information regarding at least one first individual includes information regarding mosaicism of at least one individual 640. The term "mosaicism," as used herein, denotes, for example, situations where two or more cellular subtypes arise during the lifespan of

10 an organism, situations where two or more cellular subtypes originate with the first cell of an organism and situations where the origin of the cellular subtypes is unclear. The term "mosaicism," as used herein, may include somatic mosaicism, gonadal mosaicism, or chimerism. For example, at least one aspect of epigenetic information may include information regarding mosaicism of at least one individual such as the

15 presence or absence of mosaicism, the location of mosaicism, the tissue or tissues involved in the mosaicism, or the proportion of various subtypes of cells in mosaic tissue. For more information on somatic mosaicism and disease, see Youssoufian and Pyeritz, Mechanisms and Consequences of Somatic Mosaicism in Humans, *Nature Reviews Genetics* 3: 748-758 (2002), which is incorporated herein by reference.

20 Figure 7 depicts further aspects of the system shown in Figure 5. In some embodiments, the one or more instructions for determining a similarity or a dissimilarity 520 may include one or more instructions wherein the at least one aspect of epigenetic phenotype information regarding at least one first individual includes information regarding at least one tissue source 700. For example, the information

25 regarding at least one tissue source may include information regarding the origin, storage, pathology, pathological subtype, or handling of the tissue. For example, the information regarding at least one tissue source may include information regarding at least one physical, spatial or relative anatomic source. One or more instructions 700 may include wherein the information regarding at least one tissue source includes

30 information regarding at least one abnormal tissue source 710. For example, the information regarding at least one abnormal tissue source may include information

regarding a neoplastic source, a displastic source, a diseased source, an infectious source or a cancerous source. For example, at least one aspect of epigenetic information may be associated with cancerous tissues, *e.g.* Ducasse and Brown, Epigenetic Alterations and Cancer, *Molecular Cancer* 5:60 (2006); and Kagen et al.,
5 Towards Clinical Application of Methylated DNA Sequences as Cancer Biomarkers, a Joint NCI's EDRN and NIST Workshop on Standards, Methods, Assays, Reagents and Tools, *Cancer Research* 67:4545-4549 (2007), which are incorporated herein by reference. Also by way of example, some aspects of epigenetic information may be associated with human disease diagnoses, *e.g.* Feinberg, Phenotypic Plasticity and the
10 Epigenetics of Human Disease, *Nature* 477: 433-440 (2007), which is incorporated herein by reference. One or more instructions 700 may include wherein the information regarding at least one tissue source includes information regarding at least one type of tissue 720. For example, information regarding at least one type of tissue may include information regarding at least one clinical diagnosis, at least one
15 pathology report, or at least one surgical report. For example, the information regarding at least one type of tissue may include the origin tissue type, the handling of the tissue, or one or more treatments to the tissue. In some embodiments, the information regarding at least one type of tissue may include cellular developmental stage, lineage, or status. In some embodiments, the one or more instructions for
20 determining a similarity or a dissimilarity 520 may include one or more instructions wherein the at least one epigenetic-influencing event includes at least one medical therapy 730. For example, an epigenetic-influencing event may include a medical therapy including one or more medications, or one or more treatments. An epigenetic-influencing event may include at least one medical therapy including one
25 or more energy-based procedures, for example radiation therapy, UV therapy, thermal therapy, phototherapy, or ultrasound therapy. In some embodiments, the one or more instructions for determining a similarity or a dissimilarity 520 may include one or more instructions wherein the at least one epigenetic-influencing event includes at least one environmental event 740. For example, an environmental event may
30 include exposure of an individual to radiation, one or more pollutants, or one or more toxins. For example, an environmental event may include exposure of an individual

to excessive levels of di(2-ethylhexyl)phthalate (DEHP). For example, an environmental event may include exposure of an individual to excessive levels of heavy metals, nickel, lead, cadmium, mercury, or arsenic. In some embodiments, an environmental event may include some element of activity by an individual, such as
5 when an individual goes to or stays in a location with exposures such as those described herein.

Figure 8 depicts further aspects of the system shown in Figure 5. In some embodiments, the computer program 520 may include one or more instructions for correlating the at least one aspect of epigenetic phenotype information regarding at
10 least one second individual with previous epigenetic information regarding the at least one second individual, wherein the previous epigenetic information was ascertained prior to the epigenetic-influencing event 800. In some embodiments, the one or more instructions 800 may include wherein the at least one aspect of epigenetic phenotype information is information regarding a subset of data points of
15 the previous epigenetic information 810. For example, an initial assay or group of assays may yield information regarding a large number of data points, while subsequent smaller assays or groups of assays may yield information regarding a smaller group, or subset of data points. For example, an initial assay may yield a large number of data points that are included in the system, while information from
20 further assays that is incorporated into a system is limited to a subset of data points. The computer program 510 may also include one or more instructions for suggesting at least one intervention strategy for the at least one first individual in reference to the at least one correlation 820.

Figure 9 depicts a partial view of a system that may serve as an illustrative
25 environment of or for subject matter technologies. One or more users 940 may use a system 900 including at least one computer program 910 for use with at least one computer system, wherein the at least one computer program 910 includes a plurality of instructions. One or more users 940 may include, for example, one or more administrators, medical personnel, pharmacists, geneticists, researchers or
30 technicians. Although a single user is shown in Figure 9, in some embodiments at least one group of users or at least one series of users may interact with the system.

In some embodiments, the one or more users 940 may include a computer system, artificial intelligence system (AI) or other circuitry. The at least one computer program 910 may include one or more instructions for determining one or more correlations between at least one aspect of epigenetic phenotype information obtained
5 regarding at least one individual and information regarding at least one epigenetic-influencing event in relation to the at least one first individual 920. The at least one computer program 910 may include one or more instructions for applying at least one of the one or more correlations to at least one aspect of epigenetic phenotype information regarding at least one second individual 930.

10 Figure 10 depicts further aspects of the system shown in Figure 9. In some embodiments, one or more instructions for determining one or more correlations 920 may include wherein the at least one epigenetic-influencing event includes at least one medical therapy 1000. For example, an epigenetic-influencing event may include a medical therapy including one or more medications, or one or more treatments. An
15 epigenetic-influencing event may include at least one medical therapy including one or more energy-based procedures, for example radiation therapy, UV therapy, thermal therapy, phototherapy, or ultrasound therapy. In some embodiments, one or more instructions for determining one or more correlations 920 may include wherein the at least one epigenetic-influencing event includes at least one environmental event 1010.
20 For example, an environmental event may include exposure of an individual to radiation, one or more pollutants, or one or more toxins. For example, an environmental event may include exposure of an individual to excessive levels of di(2-ethylhexyl)phthalate (DEHP). For example, an environmental event may include exposure of an individual to excessive levels of heavy metals, nickel, lead,
25 cadmium, mercury, or arsenic. In some embodiments, an environmental event may include some element of activity by an individual, such as when an individual goes to or stays in a location with exposures such as those described herein. In some embodiments, one or more instructions for determining one or more correlations 920 may include wherein the at least one aspect of epigenetic phenotype information
30 regarding at least one first individual includes information regarding DNA methylation 1020. For example, one or more instructions wherein the at least one

aspect of epigenetic phenotype information regarding at least one first individual may include information regarding the methylation status of DNA generally or in the aggregate, or information regarding DNA methylation at one or more specific DNA loci, DNA regions, or DNA bases. In some embodiments, one or more instructions
5 for determining one or more correlations 920 may include wherein the at least one aspect of epigenetic phenotype information regarding at least one first individual includes information regarding at least one tissue source 1030. For example, the information regarding at least one tissue source may include information regarding the origin, storage, pathology, pathological subtype, or handling of the tissue. For
10 example, the information regarding at least one tissue source may include information regarding at least one physical, spatial or relative anatomic source.

Figure 11 shows aspects of the system depicted in Figure 10. In some embodiments, the at least one computer program 910 may include one or more instructions for predicting at least one epigenetic-influencing event influencing the at
15 least one second individual 1100. In some embodiments, the at least one computer program 910 may include one or more instructions for suggesting at least one intervention strategy for one or more of the at least one second individual 1110. For example, one or more instructions for suggesting at least one intervention strategy may include instructions for suggesting at least one medication, therapy, treatment or
20 course of action relating to the at least one second individual.

Figure 12 depicts a partial view of a system that may serve as an illustrative environment of or for subject matter technologies. One or more users 1240 may use a system 1200 including at least one computer program 1210 for use with at least one computer system, wherein the at least one computer program 1210 includes a
25 plurality of instructions. One or more users 1240 may include, for example, one or more administrators, medical personnel, pharmacists, geneticists, researchers or technicians. Although a single user is shown in Figure 12, in some embodiments at least one group of users or at least one series of users may interact with the system. In some embodiments, the one or more users 1240 may include a computer system,
30 artificial intelligence system (AI) or other circuitry. The at least one computer program 1210 may include one or more instructions for determining one or more

correlations between at least one aspect of epigenetic phenotype information obtained regarding at least one first individual and information regarding at least one medical therapy in relation to the at least one first individual 1220. For example, a medical therapy may include one or more medications, or one or more treatments. At least one medical therapy may include one or more energy-based procedures, for example radiation therapy, UV therapy, thermal therapy, phototherapy, or ultrasound therapy. The at least one computer program 1210 may include one or more instructions for applying at least one of the one or more correlations to at least one aspect of epigenetic phenotype information regarding at least one second individual 1230.

Figure 13 shows further aspects of the system shown in Figure 12. In some embodiments, the one or more instructions for determining one or more correlations 1220 may include wherein the at least one medical therapy includes at least one therapeutic agent 1300. For example, the at least one medical therapy may include at least one therapeutic agent such as at least one drug, biologic, biological material, formulation, pharmaceutical, nutraceutical, dietary supplement, vitamin or compound. A therapeutic agent may be administered, for example, in a variety of ways including oral, topical, iv, ip, sc, intranasal, and inhalation. In some embodiments, the one or more instructions for determining one or more correlations 1220 may include wherein the at least one medical therapy includes at least one energy-based procedure 1310. For example, at least one medical therapy including one or more energy-based procedures, may include one or more of: radiation therapy, UV therapy, thermal therapy, phototherapy, or ultrasound therapy. In some embodiments, the one or more instructions for determining one or more correlations 1220 may include wherein the at least one aspect of epigenetic phenotype information regarding at least one first individual includes information regarding DNA methylation 1320. For example, at least one aspect of epigenetic phenotype information may include information regarding the methylation status of DNA generally or in the aggregate, or information regarding DNA methylation at one or more specific DNA loci, DNA regions, or DNA bases. In some embodiments, the one or more instructions for determining one or more correlations 1220 may include wherein the at least one aspect of epigenetic phenotype information regarding at least one first individual includes information

regarding at least one tissue source 1330. For example, the information regarding at least one tissue source may include information regarding the origin, storage, pathology, pathological subtype, or handling of the tissue. For example, the information regarding at least one tissue source may include information regarding at least one physical, spatial or relative anatomic source. In some embodiments, the at least one computer program 1210 may include one or more instructions for suggesting at least one intervention strategy for one or more of the at least one second individual 1340. For example, one or more instructions for suggesting at least one intervention strategy may include instructions for suggesting at least one medication, therapy, treatment or course of action relating to the at least one second individual.

Figure 14 depicts a partial view of a system that may serve as an illustrative environment of or for subject matter technologies. One or more users 1440 may use a system 1400 including at least one computer program 1410 for use with at least one computer system, wherein the at least one computer program 1410 includes a plurality of instructions. One or more users 1440 may include, for example, one or more administrators, medical personnel, pharmacists, geneticists, researchers or technicians. Although a single user is shown in Figure 14, in some embodiments at least one group of users or at least one series of users may interact with the system. In some embodiments, the one or more users 1440 may include a computer system, artificial intelligence system (AI) or other circuitry. The at least one computer program 1410 may include one or more instructions for determining one or more correlations between at least one aspect of epigenetic phenotype information obtained regarding at least one first individual and information regarding at least one environmental event in relation to the at least one first individual 1420. For example, an environmental event may include exposure of an individual to radiation, one or more pollutants, or one or more toxins. The at least one computer program 1410 may include one or more instructions for applying at least one of the one or more correlations to at least one aspect of epigenetic phenotype information regarding at least one second individual 1430.

Figure 15 illustrates further aspects of the system shown in Figure 14. In some embodiments, the one or instructions for determining one or more correlations

1420 may include wherein the at least environmental event includes at least one environmental pollutant 1500. For example, the at least one environmental event may include an environmental pollutant such as overly high levels of arsenic in drinking water. For example, the at least one environmental event may include an
5 environmental pollutant such as heavy metal particulates in the air. In some embodiments, an environmental event may include some element of activity by an individual, such as when an individual goes to or stays in a location with exposures such as those described herein. In some embodiments, the one or instructions for determining one or more correlations 1420 may include wherein the at least one
10 environmental event includes at least one toxin 1510. For example, the at least one environmental event may include at least one toxin such as released industrial wastes, unprocessed sewage, or particulates in the air, including asbestos. In some embodiments, the one or instructions for determining one or more correlations 1420 may include wherein the at least one aspect of epigenetic phenotype information
15 regarding at least one first individual includes information regarding DNA methylation 1520. For example, at least one aspect of epigenetic phenotype information may include information regarding the methylation status of DNA generally or in the aggregate, or information regarding DNA methylation at one or more specific DNA loci, DNA regions, or DNA bases. In some embodiments, the
20 one or instructions for determining one or more correlations 1420 may include wherein the at least one aspect of epigenetic phenotype information regarding at least one first individual includes information regarding at least one tissue source 1530. For example, the information regarding at least one tissue source may include information regarding the origin, storage, pathology, pathological subtype, or
25 handling of the tissue. For example, the information regarding at least one tissue source may include information regarding at least one physical, spatial or relative anatomic source.

Figure 16 depicts further aspects of the system illustrated in Figure 14. In some embodiments, at least one computer program 1410 may include one or more
30 instructions for predicting at least one environmental event influencing the at least one second individual 1600. For example, one or more instructions for predicting at

least one environmental event influencing the at least one second individual may include instructions for predicting the influence of at least one toxin or pollutant. For example, instructions for predicting the influence of at least one toxin or pollutant may include instructions for predicting changes in DNA methylation, histone
5 structure, or mosaicism of at least one individual in relation to exposure to at least one toxin or pollutant. In some embodiments, at least one computer program 1410 may include one or more instructions for suggesting at least one intervention strategy for one or more of the at least one second individual 1610. For example, one or more instructions for suggesting at least one intervention strategy may include instructions
10 for suggesting at least one medication, therapy, treatment or course of action relating to the at least one second individual.

B. Operation(s) or Process(es)

Following are a series of flowcharts depicting implementations of processes. For ease of understanding, the flowcharts are organized such that the initial
15 flowcharts present implementations via an overall “big picture” or “top-level” viewpoint and thereafter the subsequent flowcharts present alternate implementations or expansions of the “big picture” flowcharts as either sub-steps or additional steps building on one or more earlier-presented flowcharts. Those having skill in the art will appreciate that the style of presentation utilized herein (*e.g.*, beginning with a
20 presentation of a flowchart(s) presenting an overall view and thereafter providing additions to or further details in subsequent flowcharts) generally allows for a more rapid and reliable understanding of the various process implementations.

With reference now to Figure 17, illustrated is a flowchart of a method. Block 710 depicts the start of the method. Block 1700 depicts determining a similarity or
25 dissimilarity between at least one aspect of epigenetic phenotype information regarding at least one first individual and at least one aspect of epigenetic phenotype information regarding at least one second individual, wherein the at least one second individual had been influenced by the at least one epigenetic-influencing event. Block 1720 depicts the end of the method.

Figure 18 depicts alternate aspects of the flowchart illustrated in Figure 17. In some embodiments, block 1700 may include one or more of optional blocks 1800, 1810, 1820, 1830 or 1840. Block 1800 depicts wherein the at least one aspect of epigenetic phenotype information regarding at least one first individual comprises at least one aspect of epigenetic phenotype information assayed at more than one time. Block 1810 shows wherein the at least one aspect of epigenetic phenotype information regarding at least one first individual includes information regarding DNA methylation. Block 1820 illustrates wherein the at least one aspect of epigenetic phenotype information regarding at least one first individual includes information regarding histone structure. Block 1830 depicts wherein the at least one aspect of epigenetic phenotype information regarding at least one first individual includes information regarding multiple genomic loci. Block 1840 shows wherein the at least one aspect of epigenetic phenotype information regarding at least one first individual includes information regarding mosaicism of at least one first individual.

Figure 19 illustrates alternate aspects of the flowchart illustrated in Figure 17. In some embodiments, block 1700 may include one or more of optional blocks 1900, 1910, 1920, 1930 or 1940. Block 1900 depicts wherein the at least one aspect of epigenetic phenotype information regarding at least one first individual includes information regarding at least one tissue source. Block 1900 may include block 1910 illustrating wherein the information regarding at least one tissue source includes information regarding at least one abnormal tissue source. Block 1900 may include block 1910 showing wherein the information regarding at least one tissue source includes information regarding at least one type of tissue. Block 1700 may also include block 1930 depicting wherein the at least one epigenetic-influencing event includes at least one medical therapy. Block 1700 may include block 1940 showing wherein the at least one epigenetic-influencing event includes at least one environmental event.

Figure 20 depicts alternate aspects of the flowchart illustrated in Figure 17. As shown in Figure 20, the flowchart may include one or more of blocks 2000, 2010, or 2020. Block 2000 illustrates correlating the at least one aspect of epigenetic phenotype information regarding at least one second individual with previous

epigenetic information regarding the at least one second individual, wherein the previous epigenetic information was ascertained prior to the epigenetic-influencing event. Block 2000 may include block 2010, depicting wherein the at least one aspect of epigenetic information is information regarding a subset of data points of the previous epigenetic information. The flowchart may also contain block 2020, showing suggesting at least one intervention strategy for the at least one first individual in reference to the at least one correlation.

Figure 21 illustrates a flowchart of a method. Block 2110 depicts the start of the method. Block 2100 shows determining at least one correlation between at least one epigenetic-influencing event and at least one aspect of epigenetic phenotype information regarding at least one individual. Block 2120 illustrates the end of the method.

Figure 22 depicts alternate aspects of the flowchart illustrated in Figure 21. As shown in Figure 22, block 2100 may include one or more of blocks 2200, 2210, 2220, 2230, or 2240. Block 2200 depicts wherein the at least one aspect of epigenetic phenotype information regarding at least one first individual comprises at least one aspect of epigenetic phenotype information assayed at more than one time. Block 2210 illustrates wherein the at least one aspect of epigenetic phenotype information regarding at least one first individual includes information regarding DNA methylation. Block 2220 shows wherein the at least one aspect of epigenetic phenotype information regarding at least one first individual includes information regarding histone structure. Block 2230 depicts wherein the at least one aspect of epigenetic phenotype information regarding at least one first individual includes information regarding multiple genomic loci. Block 2240 shows wherein the at least one aspect of epigenetic phenotype information regarding at least one first individual includes information regarding mosaicism of at least one first individual.

Figure 23 illustrates alternate aspects of the flowchart shown in Figure 21. Block 2100 may include one or more of blocks 2300, 2310, 2320, 2330, or 2340. Block 2300 depicts wherein the at least one aspect of epigenetic phenotype information regarding at least one first individual includes information regarding at least one tissue source. Block 2300 may include one or more of blocks 2310 and

2320. Block 2310 shows wherein the information regarding at least one tissue source includes information regarding at least one abnormal tissue source. Block 2320 illustrates wherein the information regarding at least one tissue source includes information regarding at least one type of tissue. Block 2100 may also include block
5 2330. Block 2330 depicts wherein the at least one epigenetic-influencing event includes at least one medical therapy. Block 2340 shows wherein the at least one epigenetic-influencing event includes at least one environmental event.

Figure 24 depicts further aspects of the flowchart shown in Figure 21. In addition to block 2100, a flowchart of a method may also include one or more of
10 blocks 2400, 2410, or 2420. Block 2400 depicts correlating the at least one aspect of epigenetic phenotype information regarding at least one second individual with previous epigenetic information regarding the at least one second individual, wherein the previous epigenetic information was ascertained prior to the epigenetic-influencing event. Block 2400 may include block 2410. Block 2410 illustrates
15 wherein the at least one aspect of epigenetic phenotype information is information regarding a subset of data points of the previous epigenetic information. A flowchart may also include block 2420. Block 2420 shows suggesting at least one intervention strategy for the at least one first individual in reference to the at least one correlation.

Figure 25 illustrates a flowchart of a method. Block 2520 depicts the start of
20 the method. Block 2500 shows determining a similarity or a dissimilarity between at least one aspect of epigenetic phenotype information obtained regarding at least one first individual and information regarding at least one epigenetic-influencing event in relation to the at least one first individual. Block 2510 depicts applying at least one of the one or more correlations to at least one aspect of epigenetic phenotype
25 information regarding at least one second individual. Block 2530 depicts the end of the method.

Figure 26 illustrates further aspects of the flowchart depicted in Figure 25. Block 2500 may include one or more of blocks 2600, 2610, 2620, or 2630. Block 2600 depicts wherein the at least one epigenetic-influencing event includes at least
30 one medical therapy. Block 2610 shows wherein the at least one epigenetic-influencing event includes at least one environmental event. Block 2620 illustrates

wherein the at least one aspect of epigenetic phenotype information regarding at least one first individual includes information regarding DNA methylation. Block 2630 depicts wherein the at least one aspect of epigenetic phenotype information regarding at least one first individual includes information regarding at least one tissue source.

- 5 The flowchart may also include one or more of blocks 2640 and 2650. Block 2640 depicts predicting at least one epigenetic-influencing event influencing the at least one second individual. Block 2650 shows suggesting at least one intervention strategy for one or more of the at least one second individual.

- 10 Figure 27 depicts aspects of a method. Block 2720 shows the start of the method. Block 2700 illustrates determining one or more correlations between at least one aspect of epigenetic phenotype information obtained regarding at least one first individual and information regarding at least one medical therapy in relation to the at least one first individual. Block 2710 shows applying at least one of the one or more correlations to at least one aspect of epigenetic phenotype information regarding at
15 least one second individual. Block 2730 depicts the end of the method.

- Figure 28 illustrates further aspects of the flowchart depicted in Figure 27. Block 2700 may include one or more of blocks 2800, 2810, 2820, or 2830. Block 2800 depicts wherein the at least one medical therapy includes at least one therapeutic agent. Block 2810 shows wherein the at least one medical therapy includes at least
20 one energy-based procedure. Block 2820 illustrates wherein the at least one aspect of epigenetic phenotype information regarding at least one first individual includes information regarding DNA methylation. Block 2830 depicts wherein the at least one aspect of epigenetic phenotype information regarding at least one first individual includes information regarding at least one tissue source. The flowchart may also
25 include block 2840. Block 2840 illustrates suggesting at least one intervention strategy for one or more of the at least one second individual.

- Figure 29 shows aspects of a method. Block 2920 depicts the start of the method. Block 2900 illustrates determining one or more correlations between at least one aspect of epigenetic phenotype information obtained regarding at least one first
30 individual and information regarding at least one environmental event in relation to the at least one first individual. Block 2910 depicts applying at least one of the one or

more correlations to at least one aspect of epigenetic phenotype information regarding at least one second individual. Block 2930 shows the end of the method.

Figure 30 illustrates further aspects of the method shown in Figure 29. Block 2900 may include one or more of blocks 3000, 3010, 3020, or 3030. Block 3000 depicts wherein the at least one environmental event includes at least one environmental pollutant. Block 3010 shows wherein the at least one environmental event includes at least one toxin. Block 3020 illustrates wherein the at least one aspect of epigenetic phenotype information regarding at least one first individual includes information regarding DNA methylation. Block 3030 depicts wherein the at least one aspect of epigenetic phenotype information regarding at least one first individual includes information regarding at least one tissue source. The flowchart may also include at least one of blocks 3040 and 3050. Block 3040 shows predicting at least one environmental event influencing the at least one second individual. Block 3050 depicts suggesting at least one intervention strategy for one or more of the at least one second individual.

Variation(s), or Implementation(s)

Those having skill in the art will recognize that the disclosure teaches modifications of the devices, structures, and/or processes within the spirit of the teaching herein. For example, methods and systems described herein may be beneficial for monitoring at least one aspect of the epigenetic phenotype information of at least one individual during the course of therapeutic treatment with a therapeutic agent, investigational agent or surgical procedure, for example. The correlation between an aspect of epigenetic phenotype information regarding at least one individual with positive or negative clinical outcome to a therapy, such as a therapeutic agent, investigational agent or surgical procedure, for example, may be used to identify the patient population that will derive the most benefit from the therapy.

The epigenetic phenotype information of at least one individual may be assessed and processed prior to initiation of treatment with a therapeutic agent,

investigational agent or surgical procedure, for example, using the methods and systems described herein. As such, a diagnostic test or tests may be developed and used to determine the baseline epigenetic phenotype information of a individual prior to treatment or inclusion in a clinical trial (see *e.g.* Kagan, et al., Towards clinical application of methylated DNA sequences as cancer biomarkers, Cancer Res. 67:4545-4549 (2007), which is herein incorporated by reference). The baseline epigenetic phenotype information of a least one individual taken prior to treatment may be compared with known epigenetic phenotype information data collected, for example, from the scientific and medical literature and incorporated into the systems described herein. Known epigenetic phenotype information of at least one individual may be derived from persons who have been previously treated with a particular therapeutic agent, investigational agent or surgical procedure and for whom data are available regarding positive and negative response to that particular therapy. For example, aberrant DNA methylation in the promoter region of WSN, the gene associated with Werner syndrome, predicts improved survival in patients with colorectal cancer treated with the topoisomerase inhibitor irinotecan (Agrela, et al., Epigenetic inactivation of the premature aging Werner syndrome gene in human cancer, Proc. Natl. Acad. Sci. 103:8822-8827 (2006), which is herein incorporated by reference). Data regarding, for example, positive and negative outcomes are routinely collected for each individual participating in a clinical trial under guidelines regulated by, for example, the Food and Drug Administration (FDA) (see *e.g.* Good Clinical Practice in FDA-Regulated Clinical Trials; available from the FDA). The methods and systems described herein may be used to derive correlations between baseline epigenetic phenotype information of a perspective patient and positive and negative outcomes of a particular therapy. As such, a physician or other medical practitioner may use these correlations, for example to guide prescribing practices or to establish inclusion/exclusion criteria for a clinical trial.

Data derived from the scientific and/or medical literature regarding known epigenetic phenotype information and incorporated into the methods and systems described herein may indicate a strong correlation between the baseline epigenetic phenotype information of at least one individual and one or more negative treatment

outcome. As such, a diagnostic test or tests may be incorporated into the treatment regimen or clinical trial design to monitor the development and/or progression of negative outcomes correlated with individual-specific epigenetic phenotype information. For example, if increased blood pressure is correlated with specific epigenetic phenotype information and the therapy, routine use of a blood pressure monitor may be incorporated into the treatment regimen or clinical trial design. In some instances, a negative outcome of the therapy correlated with specific epigenetic phenotype information may be progressive. For instance, an individual having certain epigenetic phenotype information may be prone to liver damage as a result of therapy. Based on this information, for example, an individual may be excluded from the treatment regimen or clinical trial. Alternatively, a diagnostic test may be incorporated into the treatment regimen or clinical trial to routinely monitor, for example, liver enzymes as an indicator of potential liver damage. In some instances, a negative outcome of the therapy correlated with specific epigenetic phenotype information may be life-threatening, in which case an individual may be excluded from the treatment regimen or clinical trial.

The baseline epigenetic phenotype information of at least one individual may serve as a comparator for possible changes in epigenetic phenotype information noted through monitoring during the course of treatment and/or thereafter using the methods and systems described herein. As such, a diagnostic test or tests may be developed and used to periodically reassess the epigenetic phenotype information of at least one individual during the course of treatment, as described herein. Changes in the epigenetic information may be indicative of disease progression. For example, a number of diseases have been linked to aberrant DNA methylation including cancer, aging, inflammation, neurological disorders, and diabetes (see *e.g.* Rodenhiser & Mann, Epigenetics and human disease: translation basic biology into clinical applications, CMAJ, 174:341-348 (2006); Feinberg, Phenotypic plasticity and the epigenetics of human disease, Nature 447:433-440 (2007); Zhu & Yao, Use of DNA methylation for cancer detection and molecular classification, J. Biochem. Mol. Biol. 40:135-141 (2007); and Wren & Garner, Data-mining analysis suggests an epigenetic pathogenesis for Type 2 diabetes, J. Biomed. Biotechnol. 2005:2 104-112 (2005),

which are herein incorporated by reference). Similarly, aberrant histone deacetylation has been linked to cancer susceptibility and malignancy (Conley, et al., Targeting epigenetic abnormalities with histone deacetylase inhibitors, *Cancer*, 107:832-840 (2006), which is herein incorporated by reference).

5 Changes in the baseline epigenetic phenotype information monitored during the course of a treatment regimen or clinical trial using the methods and systems described herein may be indicative of a positive response to therapy and disease remission. For example, the efficacy of therapies that directly alter DNA methylation or histone methylation or acetylation may be indicated by changes in the epigenetic
10 phenotype information during the course of treatment. Such therapies may be useful for the treatment, for example, of cancer (Esteller, *Cancer epigenomics: DNA methylomes and histone-modification maps*, *Nat. Rev. Genet.* 8:286-298 (2007), which is herein incorporated by reference). Therapies that modulate the acetylation of histones, such as, for example, histone deacetylase (HDAC) antagonists
15 exemplified by Vorinostat (suberoylanilide hydroxamic acid), may be monitored by assessing acetylation of histone H4, for example (Conley, et al., Targeting epigenetic abnormalities with histone deacetylase inhibitors, *Cancer*, 107:832-840 (2006); and Munshi et al., Vorinostat, a histone deacetylase inhibitor, enhances the response of human tumor cells to ionizing radiation through prolongation of γ -H2AX foci, *Mol.*
20 *Cancer Ther.* 5:1967-1974 (2006), which are herein incorporated by reference). Similarly, therapies that modulate DNA methylation, such as, for example, decitabine (5-aza-2'-deoxycytidine), may be monitored by assessing changes in global methylation using a LINE1 repetitive element bisulfite/pyrosequencing assay or a liquid chromatography/mass spectrometry assay, for example (Gollob et al., Phase I
25 trial of sequential low-dose 5-aza-2'-deoxycytidine plus high-dose intravenous bolus interleukin-2 in patients with melanoma or renal cell carcinoma, *Clin. Cancer Res.* 12:4619-4617 (2006); and Liu et al., Characterization of in vitro and in vivo hypomethylating effects of decitabine in acute myeloid leukemia by a rapid, specific and sensitive LC-MS/MS method, *Nuc. Acids. Res.* 35:e31 (2007), which are herein
30 incorporated by reference). Changes in the epigenetic phenotype information of at least one individual may also occur with therapeutic treatments not known to directly

modulate chromatin function. For example, antipsychotic drugs, such as dopamine D₂-like antagonists, induce chromatin modifications in nuclei of striatal neurons, exemplified by phosphorylation and acetylation of histone H3 (Li et al., Dopamine D₂-like antagonists induce chromatin remodeling in striatal neurons through cyclic AMP-protein kinase A and NMDA receptor signaling, J. Neurochem. 90:1117-1131 (2004), which is herein incorporated by reference).

The methods and systems described herein may also be beneficial in assessing the potential toxicity of an existing or investigational therapy in an outpatient setting or during clinical trial progression (see *e.g.* Watson et al., The value of DNA methylation analysis in basic, initial toxicity assessments, Toxicol. Sci. 79:178-188 (2004), which is herein incorporated by reference). For example, the baseline epigenetic phenotype information of a individual may be determined prior to initiation of a treatment regimen or clinical trial and the data incorporated into a database accessible by the system described herein. As the treatment regimen or clinical trial proceeds, the epigenetic phenotype information may be periodically reassessed and monitored for any changes. Changes in the epigenetic phenotype information may or may not be correlated with one or more negative outcome observed during the time course of the study. Any changes in the epigenetic phenotype information may be linked back to known information regarding specific epigenetic changes and possible outcomes. For example, DNA hypermethylation in promoter regions may lead to transcriptional silencing and cancer whereas DNA hypomethylation may lead to overexpression of an oncogene and genomic instability (see *e.g.* Callinan & Feinberg, The emerging science of epigenetics, Hum. Mol. Genet. 15:R95-R101 (2006), which is herein incorporated by reference). As such, a change in the epigenetic phenotype information over the course of treatment may indicate increased risk of developing a disease in the future. For example, radiotherapy used to treat certain types of cancer is known to be associated with increased risk of secondary disease in some patients. Low-dose radiation exposure in the thymus, for example, is associated with the loss of histone H4 trimethylation and a decrease in global DNA methylation (Pogribny et al., Fractionated low-dose radiation exposure leads to accumulation of DNA damage and profound alternations

in DNA and histone methylation in the murine thymus, Mol. Cancer Res. 3:553-561 (2005), which is herein incorporated by reference). As such, changes in epigenetic phenotype information associated with radiotherapy may be used to predict the increased risk of secondary disease. In addition, changes in the epigenetic phenotype information associated with a specific treatment option can be compared, for example, with one or more agents with comparable method of action to determine if changes in epigenetic phenotype information is a class phenomenon associated with all agents possessing a similar method of action or specific to the chemical entity under investigation.

The methods and systems described herein may be used, for example, in real time to generate correlations between the epigenetic phenotype information regarding at least one individual and positive or negative clinical outcomes observed during the course of a clinical trial. It is anticipated that the methods and systems described herein may be used in conjunction with clinical data management systems, computerized or otherwise, for monitoring clinical data as regulated by, for example, the Food & Drug Administration (see *e.g.* Guidance for Industry: Computerized Systems Used in Clinical Investigations, Federal Registrar, 72:26638, May 10, 2007, which is herein incorporated by reference). As the clinical trial progresses, certain epigenetic phenotype information may correlate very early with substantial benefit to one or more subpopulations of participating individuals. The clinical trial sponsor may choose to use these correlations to modify the clinical trial design by altering, for example, the inclusion/exclusion criteria for future enrollment of participants. Similarly, as the clinical trial progresses, certain epigenetic phenotype information may correlate with the occurrence of one or more negative clinical outcome that may require additional monitoring of specific individuals, an event not originally planned for in the clinical trial design. The correlations determined during the clinical trial between therapy and epigenetic phenotype information and clinical outcome may be used, for example, to design additional clinical trials with a narrowed patient population for whom, for example, the therapy will have the most positive and least negative clinical outcome.

The methods and systems described herein may also be beneficial for predicting potential disease outcome and may aide a physician or other practitioner in developing appropriate treatment options. For example, increased global DNA methylation is associated with inflammation and increased mortality in patients with chronic kidney disease undergoing dialysis (Stenvinckel et al., J Intern Med, 261:488-499 (2007), which is herein incorporated by reference). These patients have a sharply reduced lifespan, primarily due to associated cardiovascular disease. Global hypermethylation, defined by the HpaII/MspI ratio as determined by a methylation assay, is correlated with both all-cause and cardiovascular specific mortality. In this example, developing a graded correlation between the degree of global hypermethylation and, for example, onset and time course of inflammation, cardiovascular complications, and ultimately death may aide the physician or other practitioner in predicting patient outcome and in determining appropriate treatment options.

The methods and systems described herein may be used as outlined above to develop a large body of correlative data regarding epigenetic phenotype information of at least one individual and one or more medical therapies. The epigenetic phenotype information may include, for example, information regarding gender, height, weight, diabetes status, heart disease status, medical diagnosis, results on one or more medical tests, and/or ethnic background. Information regarding at least one tissue source may include information regarding the origin, storage, pathology, pathological subtype, and/or handling of the tissue and may include information regarding a neoplastic source, a displastic source, a diseased source, an infectious source and/or a cancerous source. The epigenetic phenotype information may be correlated, for example, with the Human Epigenome Project database, which is a growing body of information regarding genome-wide DNA methylation patterns of all human genes (see *e.g.* Raykan et al., PLOS Bio. DNA methylation profiling of the human major histocompatibility complex: A pilot study for the Human Epigenome Project. 2:2170-2182 (2004), which is herein incorporated by reference). Similarly, the epigenetic phenotype information may be correlated with data retrieved, for example, from the scientific and medical literature (see *e.g.* Shames et al., A genome-

wide screen for promoter methylation in lung cancer identifies novel methylation markers for multiple malignancies, PLOS Medicine, 3:2244-2263 (2006), which is herein incorporated by reference). The epigenetic phenotype information may also be correlated with pharmacogenetic information, such as polymorphisms in genes encoding enzymes associated with drug metabolism and transport (see *e.g.* Goldstein, et al., Pharmacogenetics goes genomic, Nature Rev. Genet. 4:937-947 (2003), which is herein incorporated by reference). The accumulated correlation data may be beneficial not only for clinical trial design and progression, but also for prescribing practices following approval of a new therapy. For example, a physician or other practitioner may use the accumulated correlation data in combination with the epigenetic phenotype information of an individual to predict whether a specific medical therapy will provide a positive outcome. In addition, a physician or other practitioner may use the accumulated correlation data to predict specific negative outcomes that may be associated with a given treatment and an individual's specific epigenetic phenotype information. As such, the physician and/or individual may use these data to assess the risk/benefit associated with a particular treatment option and make decisions regarding treatment accordingly. In the instance, for example, where there are multiple therapies of a given class available to treat a specific disease or condition, the physician or other practitioner may use the accumulated correlation data for each therapy in combination with the individual's specific epigenetic phenotype information to choose the optimal treatment course.

The methods and systems described herein may be beneficial for monitoring changes in epigenetic phenotype information of at least one individual in response to exposure to environmental toxins, for example, in the workplace. As such, changes in epigenetic phenotype information over time may be used, for example, to assess the precautions that have been put in place by the employer to protect the health and safety of employees and may guide decisions regarding the need for additional precautions. For example, the carcinogenic metals nickel and cadmium are used in a number of industries including the manufacture of nickel-cadmium batteries. The toxicity associated with exposure to nickel and cadmium is due in part to aberrant DNA methylation (Sutherland & Costa, Epigenetics and the environment, Ann. N.Y.

Acad. Sci. 983:151-160 (2003); Poirier et al., The prospective role of abnormal methyl metabolism in cadmium toxicity, Environ. Health Perspect. 110:793-795 (2002); and Lee et al., Carcinogenic nickel silences gene expression by chromatin condensation and DNA methylation: a new model for epigenetic carcinogens, Mol. Cell. Biol. 15:2547-2557 (1995), which are herein incorporated by reference). As such, the epigenetic phenotype information of at least one individual may be assessed at the initiation of employment and periodically reassessed and monitored for any changes. In addition, the epigenetic phenotype information of at least one individual exposed to an environmental toxin may be correlated with occupational exposure levels as monitored, for example, by urinary concentrations of toxin routinely assessed at the end of a working shift.

The methods and systems described herein may be used to monitor environmental influences on the epigenetic phenotype information of at least one individual over a lifetime beginning, for example, with conception. Human epidemiology studies suggest that prenatal and early postnatal environmental factors influence the adult risk of developing various diseases, including cancer, cardiovascular disease, metabolic disorders, obesity and mental health disorders. Changes in epigenetic marks may be a general mechanism by which early environmental exposure induces phenotypic changes later in life (Jirtle & Skinner, Environmental epigenomics and disease susceptibility, Nat. Rev. Genet. 8:253-262 (2007), which is herein incorporated by reference). Environmental factors that have been shown to influence disease susceptibility later in life include heavy metals, abnormal nutrition such as caloric restriction, and exposure to certain chemicals. The epigenetic effects of chemical exposure to benzo(a)pyrene, orthoaminoasotoluol, dioxin, and diethylstilbestrol (DES), for example, may be carried over into the next generation. For example, exposure to vinclozolin, a fungicide commonly used in the wine industry, decreases DNA methylation in testes across three generations and results in reduced male fertility (Anway et al., Epigenetic transgenerational actions of endocrine disruptors and male fertility, Science 308:1466-1469 (2005), which is herein incorporated by reference). As such, the epigenetic phenotype information of at least one individual exposed early in development to one or more environmental

factors may be monitored over a lifetime, for example, to predict and correlate disease outcomes.

The methods and systems described herein may also be beneficial for monitoring changes in epigenetic phenotype information of at least one individual in response to unexpected exposure to environmental toxins. Unexpected exposure may constitute a single event, such as an accidental release of radiation or of a toxic gas or a liquid. Alternatively, an unexpected exposure may represent long term exposure to a toxin in the soil, water and/or air, or associated, for example, with a residence. As such, the unexpected exposure may effect a single individual or an entire community.

10 An individual, for example, may be exposed to excessive levels of di(2-ethylhexyl)phthalate (DEHP) which is a component of plastics used in common household items such as, for example, wall coverings, floor tiles, dolls, rainwear, some toys and garden hoses. DEHP is also a component of medical tubing and as such exposure to DEHP in hospitalized neonates and individuals undergoing kidney

15 dialysis can be potentially high. In animals, high levels of DEHP induces liver and testicular toxicity. The current weight of evidence suggests that DEHP toxicity is linked to an epigenetic mechanism (see, for example, Agency for Toxic Substances and Disease Registry (ATSDR), Toxicological profile for di(2-ethylhexyl)phthalate (DEHP). Atlanta, GA: U.S. Department of Health and Human Services, Public Health

20 Service (2002), which is herein incorporated by reference). As such, the epigenetic phenotype information of at least one individual may be monitored using the methods and systems described herein to assess, for example, the potential health risks of DEHP exposure.

As another example, a community may experience long term exposure to

25 drinking water contaminated with arsenic, leading to an increased risk of dermal lesions such as hyper- and hypopigmentation, peripheral neuropathy, skin cancer, bladder and lung cancers and peripheral vascular disease (see, for example, World Health Organization, Arsenic in drinking water: Background document for development of *WHO Guidelines for Drinking Water Quality*;

30 WHO/SDS/WSH/03.04/75 (2003), which is herein incorporated by reference). Chronic exposure to inorganic arsenic can induce aberrant gene expression, global

DNA hypomethylation, and hypomethylation of individual genes, for example the estrogen receptor (see, for example, Sutherland & Costa, Epigenetics and the environment, Ann. N.Y. Acad. Sci. 983:151-160 (2003) and Chen et al., chronic inorganic arsenic exposure induces hepatic global and individual gene

5 hypomethylation: implications for arsenic hepatocarcinogenesis, Carcinogenesis, 25:1779-1786 (2004), which are herein incorporated by reference). As such, the epigenetic phenotype information of at least one individual in the community may be monitored using the methods and systems described herein to assess, for example, the effect of long-term arsenic exposure.

10 The methods and systems described herein may be used as outlined above to develop a large body of correlative data regarding epigenetic phenotype information of at least one individual and one or more environmental toxins. The epigenetic phenotype information may include, for example, information regarding gender, height, weight, ethnic background, occupation, residence, lifestyle choices, and/or
15 health status. The epigenetic phenotype information from a least one individual may be correlated, for example, with the Human Epigenome Project database which is a growing body of information regarding genome-wide DNA methylation patterns of all human genes (see *e.g.* Raykan et al., PLOS Bio. DNA methylation profiling of the human major histocompatibility complex: A pilot study for the Human Epigenome
20 Project. 2:2170-2182 (2004), which is herein incorporated by reference). The epigenetic phenotype information may also be correlated with information regarding specific environmental toxins and health hazards available, for example, from the Department of Health and Human Services, Agency for Toxic Substances & Disease Registry (ATSDR). The accumulated data may be beneficial not only for monitoring
25 epigenetic phenotype information associated with potential health risks of known environmental toxins, but also for identifying new toxins.

Other modifications of the subject matter herein will be appreciated by one of ordinary skill in the art in light of the teachings herein. While various aspects and embodiments have been disclosed herein, other aspects and embodiments will be
30 apparent to those skilled in the art.

Those having skill in the art will recognize that the state of the art has progressed to the point where there is little distinction left between hardware and software implementations of aspects of systems; the use of hardware or software is generally (but not always, in that in certain contexts the choice between hardware and software can become significant) a design choice representing cost vs. efficiency tradeoffs. Those having skill in the art will appreciate that there are various vehicles by which processes or systems or other technologies described herein can be effected (*e.g.*, hardware, software, or firmware), and that the preferred vehicle will vary with the context in which the processes or systems or other technologies are deployed. For example, if an implementer determines that speed and accuracy are paramount, the implementer may opt for a mainly hardware or firmware vehicle; alternatively, if flexibility is paramount, the implementer may opt for a mainly software implementation; or, yet again alternatively, the implementer may opt for some combination of hardware, software, or firmware. Hence, there are several possible vehicles by which the processes or devices or other technologies described herein may be effected, none of which is inherently superior to the other in that any vehicle to be utilized is a choice dependent upon the context in which the vehicle will be deployed and the specific concerns (*e.g.*, speed, flexibility, or predictability) of the implementer, any of which may vary. Those skilled in the art will recognize that optical aspects of implementations will typically employ optically-oriented hardware, software, and or firmware.

In a general sense, those skilled in the art will recognize that the various aspects described herein which can be implemented, individually or collectively, by a wide range of hardware, software, firmware, or any combination thereof can be viewed as being composed of various types of "electrical circuitry." Consequently, as used herein "electrical circuitry" includes, but is not limited to, electrical circuitry having at least one discrete electrical circuit, electrical circuitry having at least one integrated circuit, electrical circuitry having at least one application specific integrated circuit, electrical circuitry forming a general purpose computing device configured by a computer program (*e.g.*, a general purpose computer configured by a computer program which at least partially carries out processes or devices described

herein, or a microprocessor configured by a computer program which at least partially carries out processes or devices described herein), electrical circuitry forming a memory device (*e.g.*, forms of random access memory), or electrical circuitry forming a communications device (*e.g.*, a modem, communications switch, or optical-electrical equipment). Those having skill in the art will recognize that the subject matter described herein may be implemented in an analog or digital fashion or some combination thereof.

One skilled in the art will recognize that the herein described components (*e.g.*, steps), devices, and objects and the discussion accompanying them are used as examples for the sake of conceptual clarity and that various configuration modifications are within the skill of those in the art. Consequently, as used herein, the specific exemplars set forth and the accompanying discussion are intended to be representative of their more general classes. In general, use of any specific exemplar herein is also intended to be representative of its class, and the non-inclusion of such specific components (*e.g.*, steps), devices, and objects herein should not be taken as indicating that limitation is desired.

The herein described subject matter sometimes illustrates different components contained within, or connected with, different other components. It is to be understood that such depicted architectures are merely exemplary, and that in fact many other architectures can be implemented which achieve the same functionality. In a conceptual sense, any arrangement of components to achieve the same functionality is effectively “associated” such that the desired functionality is achieved. Hence, any two components herein combined to achieve a particular functionality can be seen as “associated with” each other such that the desired functionality is achieved, irrespective of architectures or intermedial components. Likewise, any two components so associated can also be viewed as being “operably connected,” or “operably coupled,” to each other to achieve the desired functionality, and any two components capable of being so associated can also be viewed as being “operably couplable,” to each other to achieve the desired functionality. Specific examples of operably couplable include but are not limited to physically mateable or

physically interacting components or wirelessly interactable or wirelessly interacting components or logically interacting or logically interactable components.

While particular aspects of the present subject matter described herein have been shown and described, it will be apparent to those skilled in the art that, based upon the teachings herein, changes and modifications may be made without departing from the subject matter described herein and its broader aspects and, therefore, the appended claims are to encompass within their scope all such changes and modifications as are within the true spirit and scope of the subject matter described herein. Furthermore, it is to be understood that the invention is defined by the appended claims. It will be understood by those within the art that, in general, terms used herein, and especially in the appended claims (*e.g.*, bodies of the appended claims) are generally intended as “open” terms (*e.g.*, the term “including” should be interpreted as “including but not limited to,” the term “having” should be interpreted as “having at least,” the term “includes” should be interpreted as “includes but is not limited to,” etc.). It will be further understood by those within the art that if a specific number of an introduced claim recitation is intended, such an intent will be explicitly recited in the claim, and in the absence of such recitation no such intent is present. For example, as an aid to understanding, the following appended claims may contain usage of the introductory phrases “at least one” and “one or more” to introduce claim recitations. However, the use of such phrases should not be construed to imply that the introduction of a claim recitation by the indefinite articles “a” or “an” limits any particular claim containing such introduced claim recitation to inventions containing only one such recitation, even when the same claim includes the introductory phrases “one or more” or “at least one” and indefinite articles such as “a” or “an” (*e.g.*, “a” or “an” should typically be interpreted to mean “at least one” or “one or more”); the same holds true for the use of definite articles used to introduce claim recitations. In addition, even if a specific number of an introduced claim recitation is explicitly recited, those skilled in the art will recognize that such recitation should typically be interpreted to mean *at least* the recited number (*e.g.*, the bare recitation of “two recitations,” without other modifiers, typically means *at least* two recitations, or *two or more* recitations). Furthermore, in those instances where a convention analogous

to “at least one of A, B, and C, etc.” is used, in general such a construction is intended in the sense one having skill in the art would understand the convention (*e.g.*, “ a system having at least one of A, B, and C” would include but not be limited to systems that have A alone, B alone, C alone, A and B together, A and C together, B
5 and C together, or A, B, and C together, etc.). In those instances where a convention analogous to “at least one of A, B, or C, etc.” is used, in general such a construction is intended in the sense one having skill in the art would understand the convention (*e.g.*, “ a system having at least one of A, B, or C” would include but not be limited to systems that have A alone, B alone, C alone, A and B together, A and C together, B
10 and C together, or A, B, and C together, etc.). It will be further understood by those within the art that virtually any disjunctive word or phrase presenting two or more alternative terms, whether in the description, claims, or drawings, should be understood to contemplate the possibilities of including one of the terms, either of the terms, or both terms. For example, the phrase “A or B” will be understood to include
15 the possibilities of “A” or “B” or “A and B.”

With respect to the appended claims, those skilled in the art will appreciate that recited operations therein may generally be performed in any order. Examples of such alternate orderings may include overlapping, interleaved, interrupted, reordered, incremental, preparatory, supplemental, simultaneous, reverse, or other variant
20 orderings, unless context dictates otherwise. With respect to context, even terms like “responsive to,” “related to,” or other past-tense adjectives are generally not intended to exclude such variants, unless context dictates otherwise.

With respect to the use of substantially any plural or singular terms herein, those having skill in the art can translate from the plural to the singular or from the
25 singular to the plural as is appropriate to the context or application. The various singular/plural permutations are not expressly set forth herein for sake of clarity.

All of the above U.S. patents, U.S. patent application publications, U.S. patent applications, foreign patents, foreign patent applications and non-patent publications referred to in this specification or listed in any Application Data Sheet, are
30 incorporated herein by reference, to the extent not inconsistent herewith.

The foregoing detailed description has set forth various embodiments of the devices or processes via the use of block diagrams, flowcharts, or examples. Insofar as such block diagrams, flowcharts, or examples contain one or more functions or operations, it will be understood by those within the art that each function or operation within such block diagrams, flowcharts, or examples can be implemented, individually or collectively, by a wide range of hardware, software, firmware, or virtually any combination thereof. In one embodiment, several portions of the subject matter described herein may be implemented via Application Specific Integrated Circuits (ASICs), Field Programmable Gate Arrays (FPGAs), digital signal processors (DSPs), or other integrated formats. However, those skilled in the art will recognize that some aspects of the embodiments disclosed herein, in whole or in part, can be equivalently implemented in integrated circuits, as one or more computer programs running on one or more computers (*e.g.*, as one or more programs running on one or more computer systems), as one or more programs running on one or more processors (*e.g.*, as one or more programs running on one or more microprocessors), as firmware, or as virtually any combination thereof, and that designing the circuitry or writing the code for the software and or firmware would be well within the skill of one of skill in the art in light of this disclosure. In addition, those skilled in the art will appreciate that the mechanisms of the subject matter described herein are capable of being distributed as a program product in a variety of forms, and that an illustrative embodiment of the subject matter described herein applies regardless of the particular type of signal bearing medium used to actually carry out the distribution. Examples of a signal bearing medium include, but are not limited to, the following: a recordable type medium such as a floppy disk, a hard disk drive, a Compact Disc (CD), a Digital Video Disk (DVD), a digital tape, a computer memory, etc.; and a transmission type medium such as a digital or an analog communication medium (*e.g.*, a fiber optic cable, a waveguide, a wired communications link, a wireless communication link, etc.).

The various aspects and embodiments disclosed herein are for purposes of illustration and are not intended to be limiting, with the true scope and spirit being indicated by the following claims.

Although specific dependencies have been identified in the claims, it is to be noted that all possible combinations of the features of the claims are envisaged in the present application, and therefore the claims are to be interpreted to include all possible multiple dependencies.

CLAIMS

1. A method comprising:
determining a similarity or a dissimilarity between at least one aspect of epigenetic phenotype information regarding at least one first individual and at least one aspect of epigenetic phenotype information regarding at least one second individual, wherein the at least one second individual had been influenced by at least one epigenetic-influencing event.
2. The method of claim 1, wherein the at least one aspect of epigenetic phenotype information regarding at least one first individual comprises:
at least one aspect of epigenetic phenotype information assayed at more than one time.
3. The method of claim 1, wherein the at least one aspect of epigenetic phenotype information regarding at least one first individual includes information regarding at least one of:
DNA methylation;
histone structure;
multiple genomic loci;
mosaicism of the at least one first individual; or
at least one tissue source.
4. The method of claim 1, wherein the at least one aspect of epigenetic phenotype information regarding at least one first individual includes information regarding at least one tissue source, wherein the information regarding at least one tissue source includes information regarding at least one of:
at least one abnormal tissue source; or
at least one type of tissue.

5. The method of claim 1, wherein the at least one epigenetic-influencing event includes at least one of:
 - at least one medical therapy; or
 - at least one environmental event;
6. The method of claim 1, further comprising:
 - correlating the at least one aspect of epigenetic phenotype information regarding at least one second individual with previous epigenetic information regarding the at least one second individual, wherein the previous epigenetic information was ascertained prior to the epigenetic-influencing event.
7. The method of claim 6, wherein the at least one aspect of epigenetic phenotype information is information regarding a subset of data points of the previous epigenetic information.
8. The method of claim 1, further comprising:
 - suggesting at least one intervention strategy for the at least one first individual in reference to the at least one correlation.
9. A system comprising at least one computer program for use with at least one computer system and wherein the computer program includes a plurality of instructions, including but not limited to:
 - one or more instructions for determining at least one correlation between at least one epigenetic-influencing event and at least one aspect of epigenetic phenotype information regarding at least one individual.
10. The system of claim 9, wherein the at least one aspect of epigenetic phenotype information regarding at least one individual comprises:
 - at least one aspect of epigenetic phenotype information assayed at more than one time.

11. The system of claim 9, wherein the at least one aspect of epigenetic phenotype information regarding at least one individual includes information regarding at least one of:
- DNA methylation;
 - histone structure;
 - multiple genomic loci;
 - mosaicism of at least one individual; or
 - at least one tissue source.
12. The system of claim 9, wherein the at least one aspect of epigenetic phenotype information regarding at least one individual includes information regarding at least one tissue source, wherein the information regarding at least one tissue source includes information regarding at least one of:
- at least one abnormal tissue source; or
 - at least one type of tissue.
13. The system of claim 9, wherein the at least one epigenetic-influencing event includes at least one of:
- at least one medical therapy; or
 - at least one environmental event.
14. The system of claim 9, further comprising:
- one or more instructions for correlating the at least one aspect of epigenetic phenotype information regarding at least one individual with previous epigenetic information regarding the at least one individual, wherein the previous epigenetic information was ascertained prior to the epigenetic-influencing event.
15. The system of claim 9, wherein the at least one aspect of epigenetic phenotype information is information regarding a subset of data points of the previous epigenetic information.

16. The system of claim 9, further comprising:
one or more instructions for suggesting at least one intervention strategy for the at least one first individual in reference to the at least one correlation.
17. A system comprising at least one computer program for use with at least one computer system and wherein the computer program includes a plurality of instructions, including but not limited to:
one or more instructions for determining a similarity or a dissimilarity between at least one aspect of epigenetic phenotype information regarding at least one first individual and at least one aspect of epigenetic phenotype information regarding at least one second individual, wherein the at least one second individual had been influenced by at least one epigenetic-influencing event.
18. The system of claim 17, wherein the at least one aspect of epigenetic phenotype information regarding at least one first individual comprises:
at least one aspect of epigenetic phenotype information assayed at more than one time.
19. The system of claim 17, wherein the at least one aspect of epigenetic phenotype information regarding at least one first individual includes information regarding at least one of:
DNA methylation;
histone structure;
multiple genomic loci;
mosaicism of at least one individual; or
at least one tissue source.

20. The system of claim 17, wherein the at least one aspect of epigenetic phenotype information regarding at least one first individual includes information regarding at least one tissue source, wherein the information regarding at least one tissue source includes information regarding at least one of:

- at least one abnormal tissue source; or
- at least one type of tissue.

21. The system of claim 17, wherein the at least one epigenetic-influencing event includes at least one of:

- at least one medical therapy; or
- at least one environmental event.

22. The system of claim 17, further comprising:

one or more instructions for correlating the at least one aspect of epigenetic phenotype information regarding at least one second individual with previous epigenetic information regarding the at least one second individual, wherein the previous epigenetic information was ascertained prior to the epigenetic-influencing event.

23. The system of claim 22, wherein the at least one aspect of epigenetic phenotype information is information regarding a subset of data points of the previous epigenetic information.

24. The system of claim 17, further comprising:

one or more instructions for suggesting at least one intervention strategy for the at least one first individual in reference to the at least one correlation.

25. A system comprising at least one computer program for use with at least one computer system and wherein the computer program includes a plurality of instructions, including but not limited to:
- one or more instructions for determining one or more correlations between at least one aspect of epigenetic phenotype information obtained regarding at least one first individual and information regarding at least one epigenetic-influencing event in relation to the at least one first individual; and
 - one or more instructions for applying at least one of the one or more correlations to at least one aspect of epigenetic phenotype information regarding at least one second individual.
26. The system of claim 25, wherein the at least one epigenetic-influencing event includes at least one of:
- at least one medical therapy; or
 - at least one environmental event.
27. The system of claim 25, wherein the at least one aspect of epigenetic phenotype information regarding at least one first individual includes information regarding at least one of:
- DNA methylation;
 - at least one tissue source.
28. The system of claim 25, further comprising:
- one or more instructions for predicting at least one epigenetic-influencing event influencing the at least one second individual.
29. The system of claim 25, further comprising:
- one or more instructions for suggesting at least one intervention strategy for one or more of the at least one second individual.

30. A system comprising at least one computer program for use with at least one computer system and wherein the computer program includes a plurality of instructions, including but not limited to:
- one or more instructions for determining one or more correlations between at least one aspect of epigenetic phenotype information obtained regarding at least one first individual and information regarding at least one medical therapy in relation to the at least one first individual; and
 - one or more instructions for applying at least one of the one or more correlations to at least one aspect of epigenetic phenotype information regarding at least one second individual.
31. The system of claim 30, wherein the at least one medical therapy includes at least one of:
- at least one therapeutic agent; or
 - at least one energy-based procedure.
32. The system of claim 30, wherein the at least one aspect of epigenetic phenotype information regarding at least one first individual includes information regarding at least one of:
- DNA methylation;
 - at least one tissue source.
33. The system of claim 30, further comprising:
- one or more instructions for suggesting at least one intervention strategy for one or more of the at least one second individual.

34. A system comprising at least one computer program for use with at least one computer system and wherein the computer program includes a plurality of instructions, including but not limited to:
- one or more instructions for determining one or more correlations between at least one aspect of epigenetic phenotype information obtained regarding at least one first individual and information regarding at least one environmental event in relation to the at least one first individual; and
 - one or more instructions for applying at least one of the one or more correlations to at least one aspect of epigenetic phenotype information regarding at least one second individual.
35. The system of claim 34, wherein the at least one environmental event includes at least one of:
- at least one environmental pollutant; or
 - at least one toxin.
36. The system of claim 34, wherein the at least one aspect of epigenetic phenotype information regarding at least one first individual includes information regarding at least one of:
- DNA methylation; or
 - at least one tissue source.
37. The system of claim 34, further comprising:
- one or more instructions for predicting at least one environmental event influencing the at least one second individual.
38. The system of claim 34, further comprising:
- one or more instructions for suggesting at least one intervention strategy for one or more of the at least one second individual.

FIG. 1
1/30

100 A system

110

At least one computer program for use with at least one computer system and wherein the computer program includes a plurality of instructions, including but not limited to

120

One or more instructions for determining at least one correlation between at least one epigenetic-influencing event and at least one aspect of epigenetic phenotype information regarding at least one individual



130

FIG. 2
2/30

100 A system

110 At least one computer program for use with at least one computer system and wherein the computer program includes a plurality of instructions, including but not limited to

120 One or more instructions for determining at least one correlation between at least one epigenetic-influencing event and at least one aspect of epigenetic phenotype information regarding at least one individual

200

Wherein the at least one aspect of epigenetic phenotype information regarding at least one individual comprises at least one aspect of epigenetic phenotype information assayed at more than one time

210

Wherein the at least one aspect of epigenetic phenotype information regarding at least one individual includes information regarding DNA methylation

220

Wherein the at least one aspect of epigenetic phenotype information regarding at least one individual includes information regarding histone structure

230

Wherein the at least one aspect of epigenetic phenotype information regarding an individual includes information regarding multiple genomic loci

240

Wherein the at least one aspect of epigenetic phenotype information regarding at least one individual includes information regarding mosaicism of at least one individual

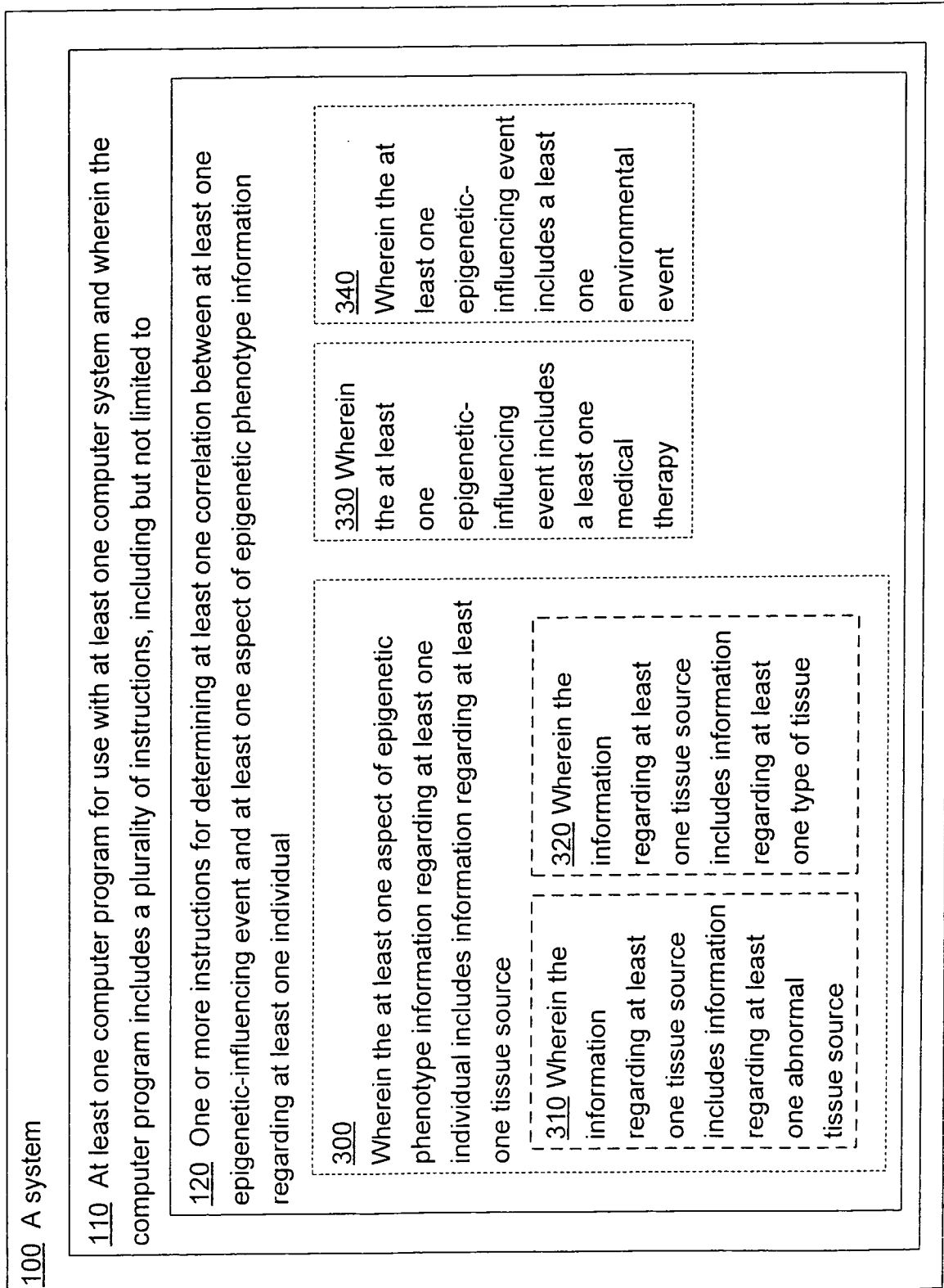
FIG. 3
3/30

FIG. 4
4/30

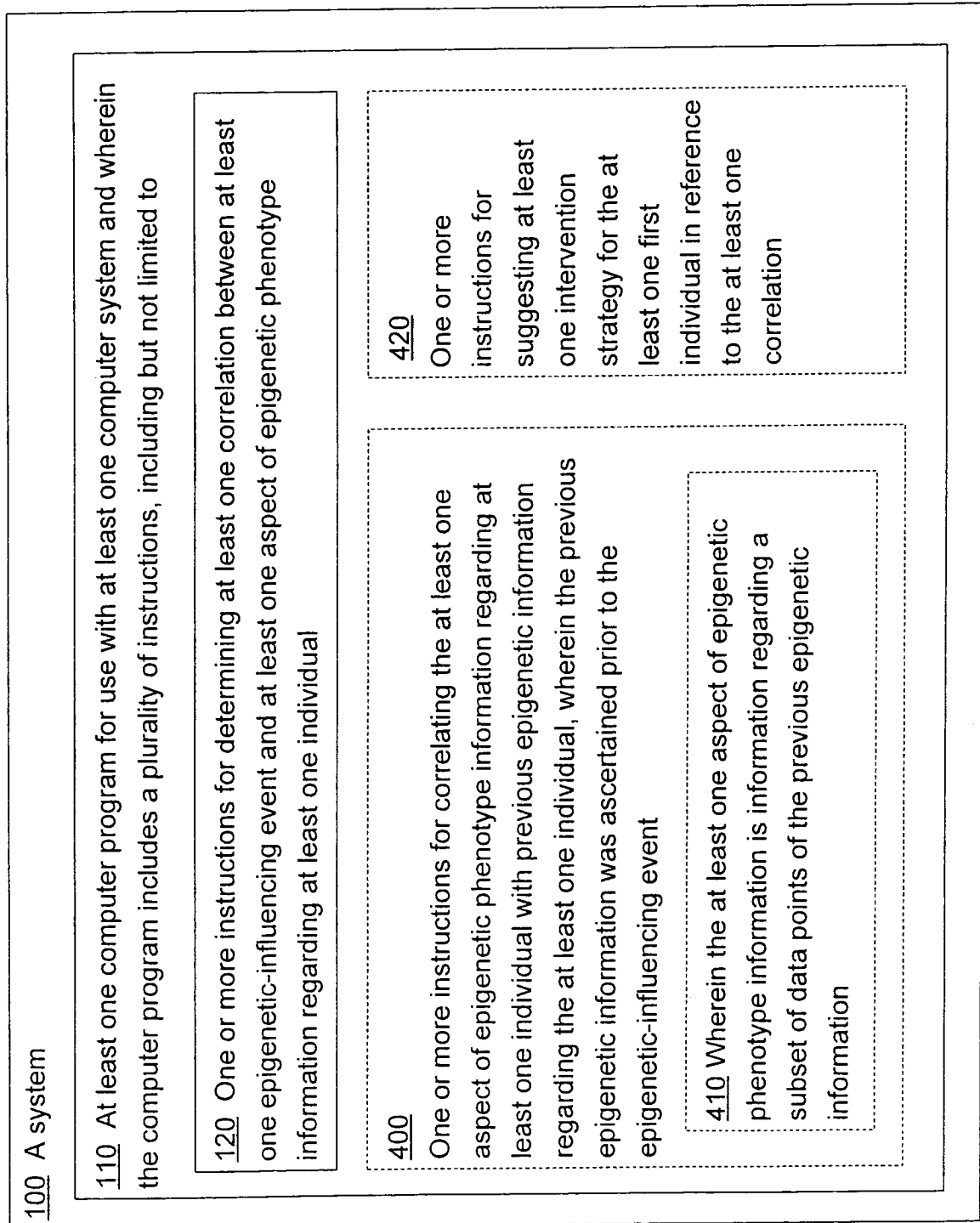


FIG. 5
5/30

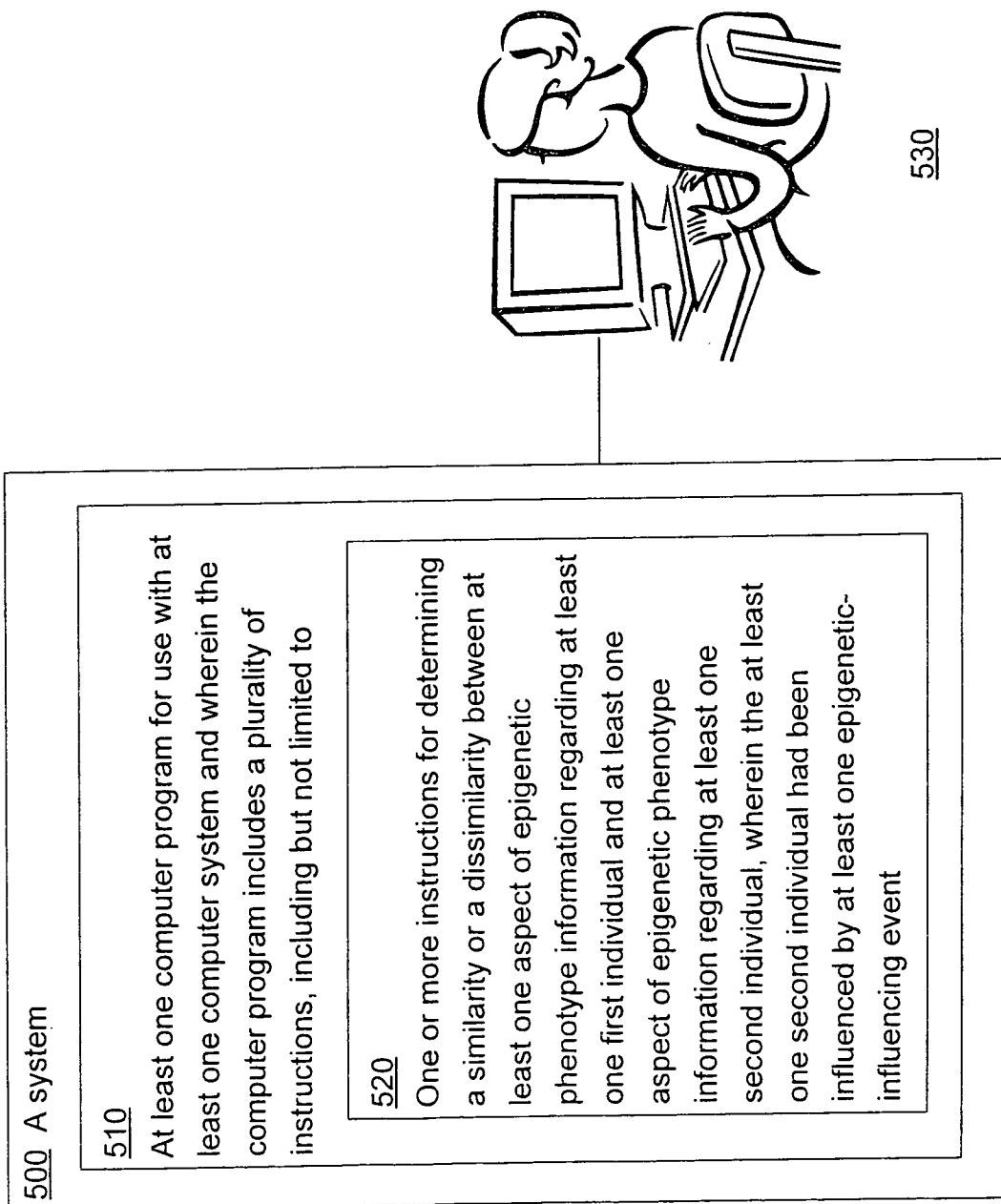


FIG. 6
6/30

500 A system

510

At least one computer program for use with at least one computer system and wherein the computer program includes a plurality of instructions, including but not limited to

520

One or more instructions for determining a similarity or a dissimilarity between at least one aspect of epigenetic phenotype information regarding at least one first individual and at least one aspect of epigenetic phenotype information regarding at least one second individual, wherein the at least one second individual had been influenced by at least one epigenetic-influencing event

600 Wherein the at least one aspect of epigenetic phenotype information regarding at least one first individual comprises at least one aspect of epigenetic phenotype information assayed at more than one time

610 Wherein the at least one aspect of epigenetic phenotype information regarding at least one first individual includes information regarding DNA methylation

620 Wherein the at least one aspect of epigenetic phenotype information regarding at least one first individual includes information regarding histone structure

630 Wherein the at least one aspect of epigenetic phenotype information regarding at least one first individual includes information regarding multiple genomic loci

640 Wherein the at least one aspect of epigenetic phenotype information regarding at least one first individual includes information regarding mosaicism of at least one individual

FIG. 7
7/30

500 A system

510

At least one computer program for use with at least one computer system and wherein the computer program includes a plurality of instructions, including but not limited to

520

One or more instructions for determining a similarity or a dissimilarity between at least one aspect of epigenetic phenotype information regarding at least one first individual and at least one aspect of epigenetic phenotype information regarding at least one second individual, wherein the at least one second individual had been influenced by at least one epigenetic-influencing event

700

Wherein the at least one aspect of epigenetic phenotype information regarding at least one first individual includes information regarding at least one tissue source

710

Wherein the information regarding at least one tissue source includes information regarding at least one abnormal tissue source

720

Wherein the information regarding at least one tissue source includes information regarding at least one type of tissue

730

Wherein the at least one epigenetic-influencing event includes at least one medical therapy

740

Wherein the at least one epigenetic-influencing event includes at least one environmental event

FIG. 8
8/30

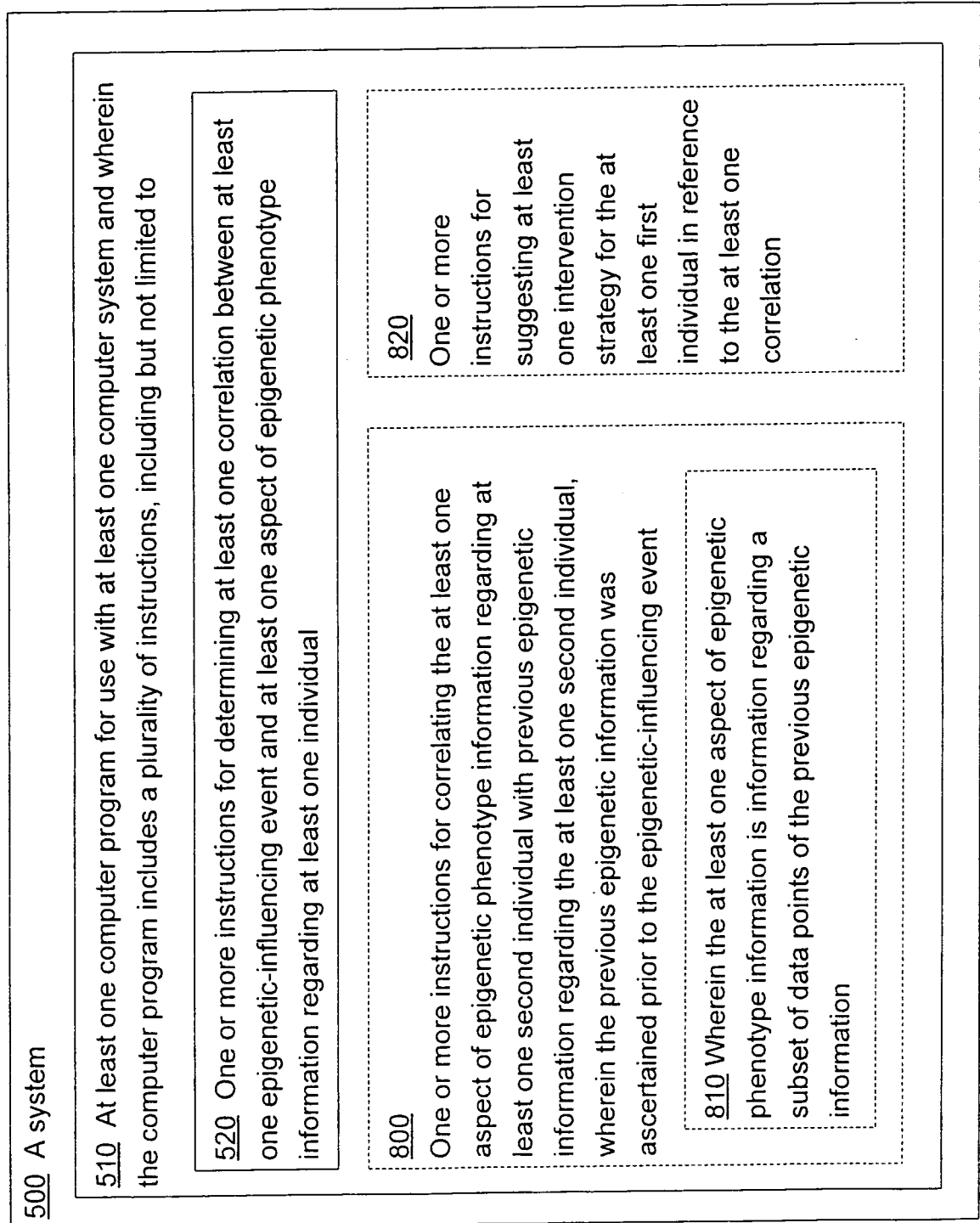


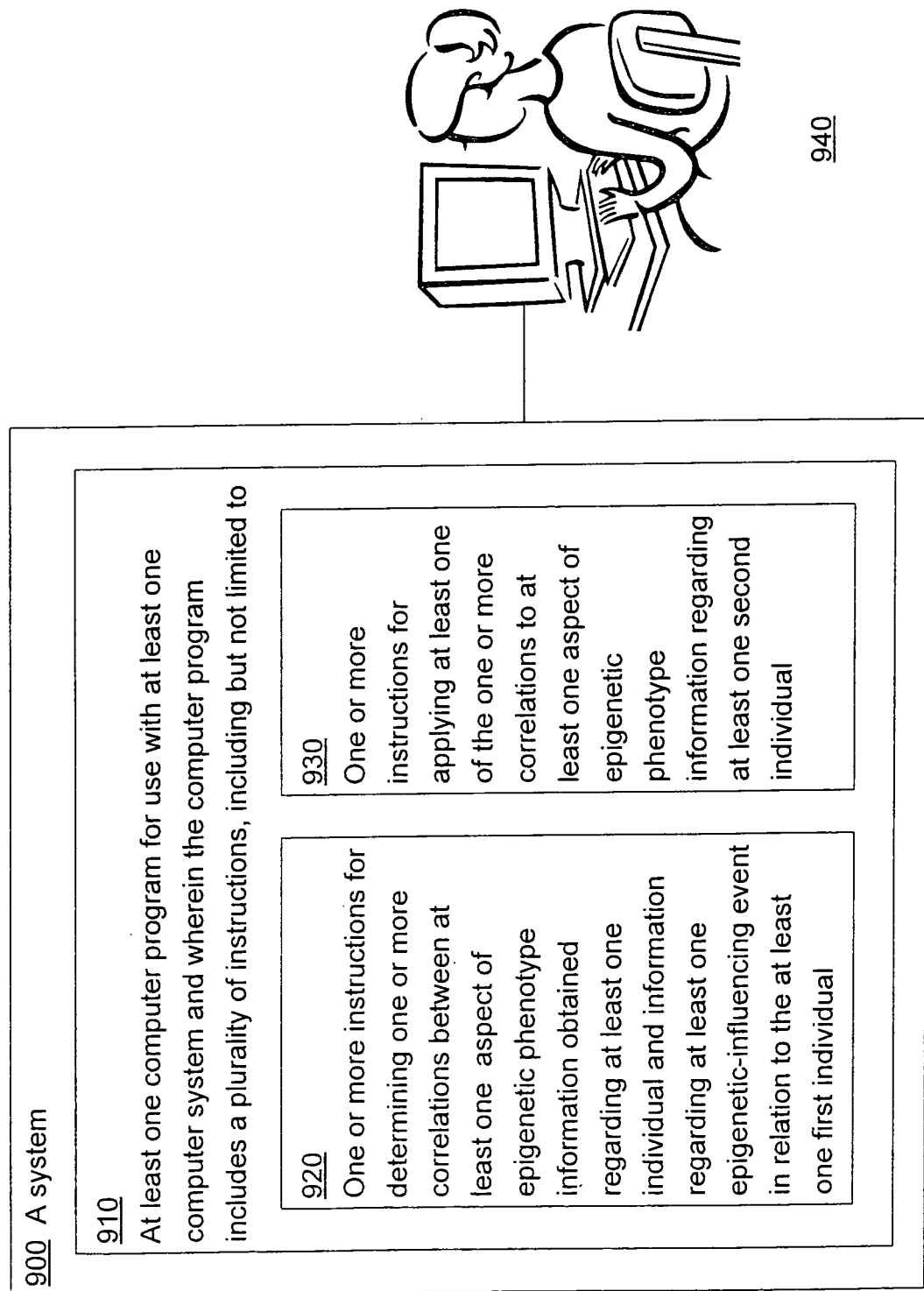
FIG. 9
9/30

FIG. 10
10/30

900 A system

910 At least one computer program for use with at least one computer system and wherein the computer program includes a plurality of instructions, including but not limited to

920

One or more instructions for determining one or more correlations between at least one aspect of epigenetic phenotype information obtained regarding at least one individual and information regarding at least one epigenetic-influencing event in relation to the at least one first individual

1000

Wherein the at least one epigenetic-influencing event includes at least one medical therapy

1010

Wherein the at least one epigenetic-influencing event includes at least one environmental event

1020

Wherein the at least one aspect of epigenetic phenotype information regarding at least one first individual includes information regarding DNA methylation

1030

Wherein the at least one aspect of epigenetic phenotype information regarding at least one first individual includes information regarding at least one tissue source

930

One or more instructions for applying at least one of the one or more correlations to at least one aspect of epigenetic phenotype information regarding at least one second individual

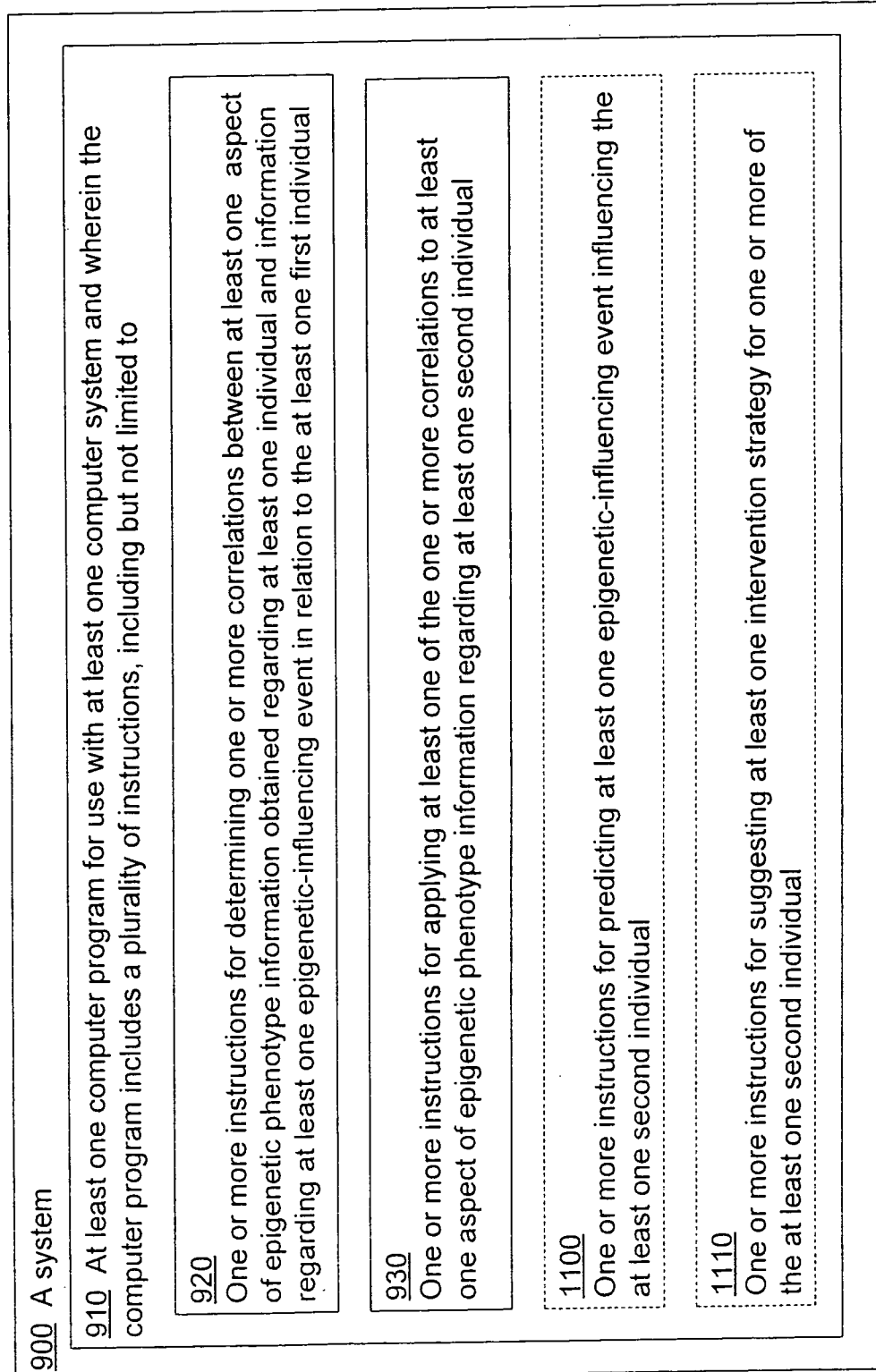
FIG. 11
11/30

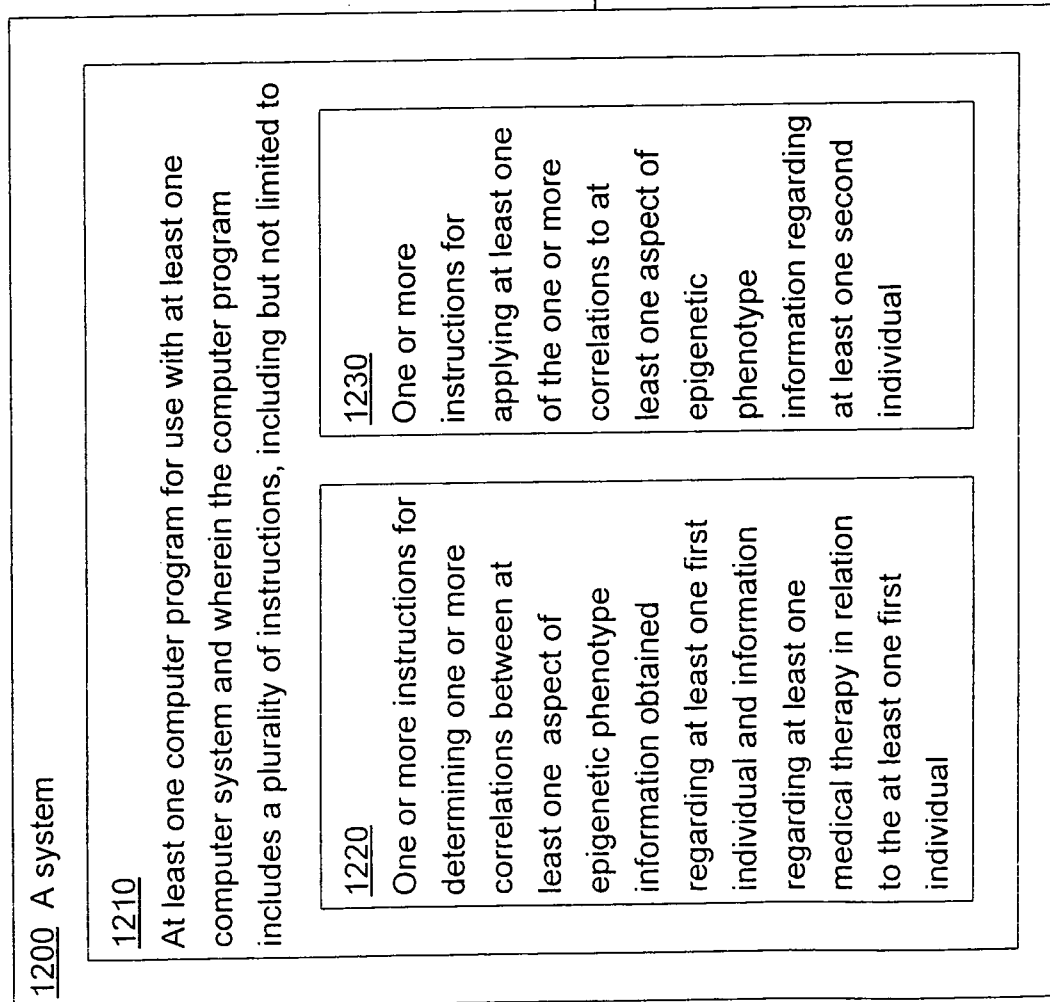
FIG. 12
12/30

FIG. 13
13/30

1200 A system

1210 At least one computer program for use with at least one computer system and wherein the computer program includes a plurality of instructions, including but not limited to

1220

One or more instructions for determining one or more correlations between at least one aspect of epigenetic phenotype information obtained regarding at least one first individual and information regarding at least one medical therapy in relation to the at least one first individual

1300

Wherein the at least one medical therapy includes at least one therapeutic agent

1310

Wherein the at least one medical therapy includes at least one energy-based procedure

1320

Wherein the at least one aspect of epigenetic phenotype information regarding at least one first individual includes information regarding DNA methylation

1330

Wherein the at least one aspect of epigenetic phenotype information regarding at least one first individual includes information regarding at least one tissue source

1230

One or more instructions for applying at least one of the one or more correlations to at least one aspect of epigenetic phenotype information regarding at least one second individual

1340

One or more instructions for suggesting at least one intervention strategy for one or more of the at least one second individual

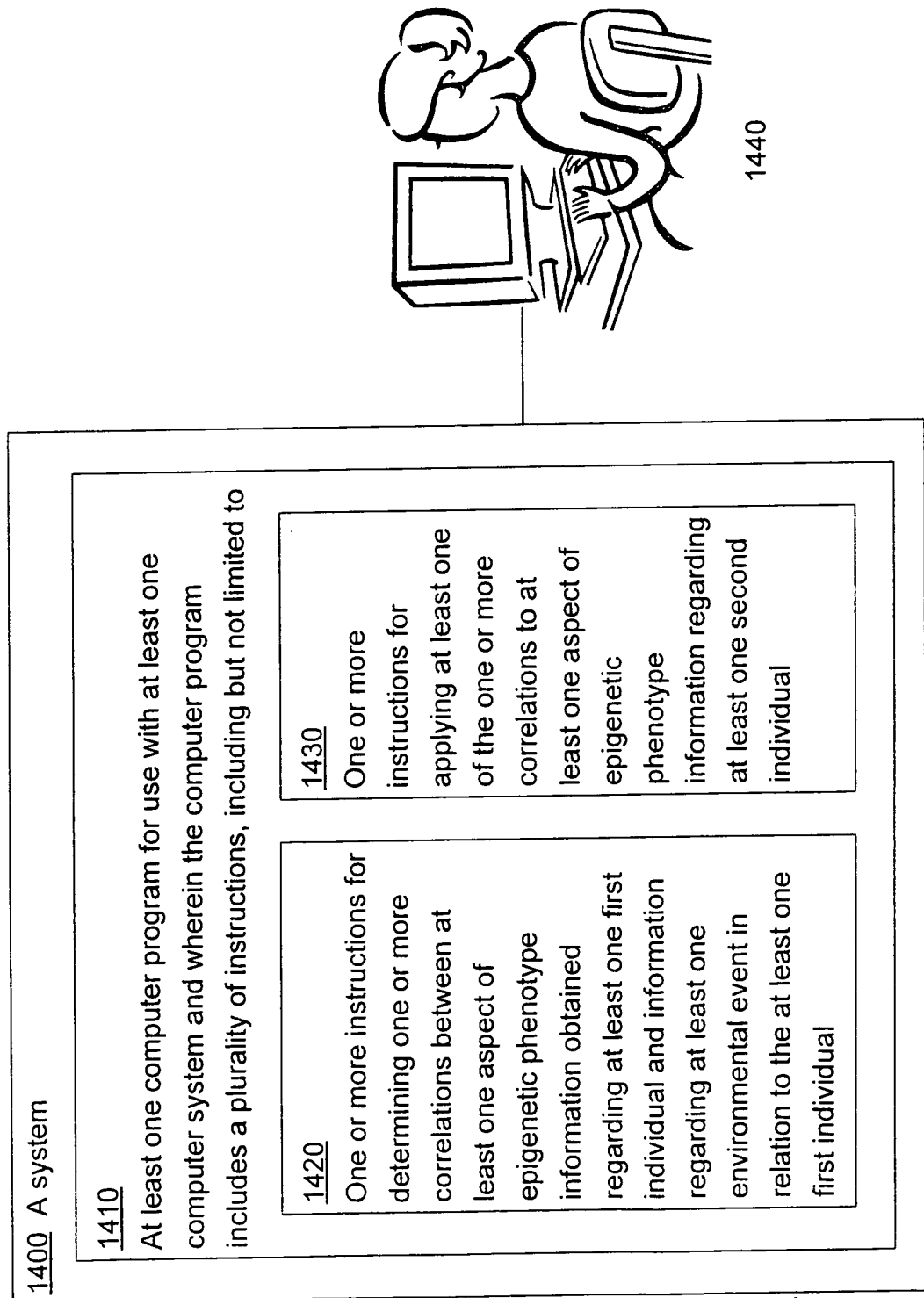
FIG. 14
14/30

FIG. 15
15/30

1400 A system

1410 At least one computer program for use with at least one computer system and wherein the computer program includes a plurality of instructions, including but not limited to

1420

One or more instructions for determining one or more correlations between at least one aspect of epigenetic phenotype information obtained regarding at least one first individual and information regarding at least one environmental event in relation to the at least one first individual

1500

Wherein the at least one environmental event includes at least one environmental pollutant

1510

Wherein the at least one environmental event includes at least one toxin

1520

Wherein the at least one aspect of epigenetic phenotype information regarding at least one first individual includes information regarding DNA methylation

1530

Wherein the at least one aspect of epigenetic phenotype information regarding at least one first individual includes information regarding at least one tissue source

1430

One or more instructions for applying at least one of the one or more correlations to at least one aspect of epigenetic phenotype information regarding at least one second individual

FIG. 16
16/30

1400 A system

1410 At least one computer program for use with at least one computer system and wherein the computer program includes a plurality of instructions, including but not limited to

1420

One or more instructions for determining one or more correlations between at least one aspect of epigenetic phenotype information obtained regarding at least one first individual and information regarding at least one medical therapy in relation to the at least one first individual

1430

One or more instructions for applying at least one of the one or more correlations to at least one aspect of epigenetic phenotype information regarding at least one second individual

1600

One or more instructions for predicting at least one environmental event influencing the at least one second individual

1610

One or more instructions for suggesting at least one intervention strategy for one or more of the at least one second individual

FIG. 17
17/30

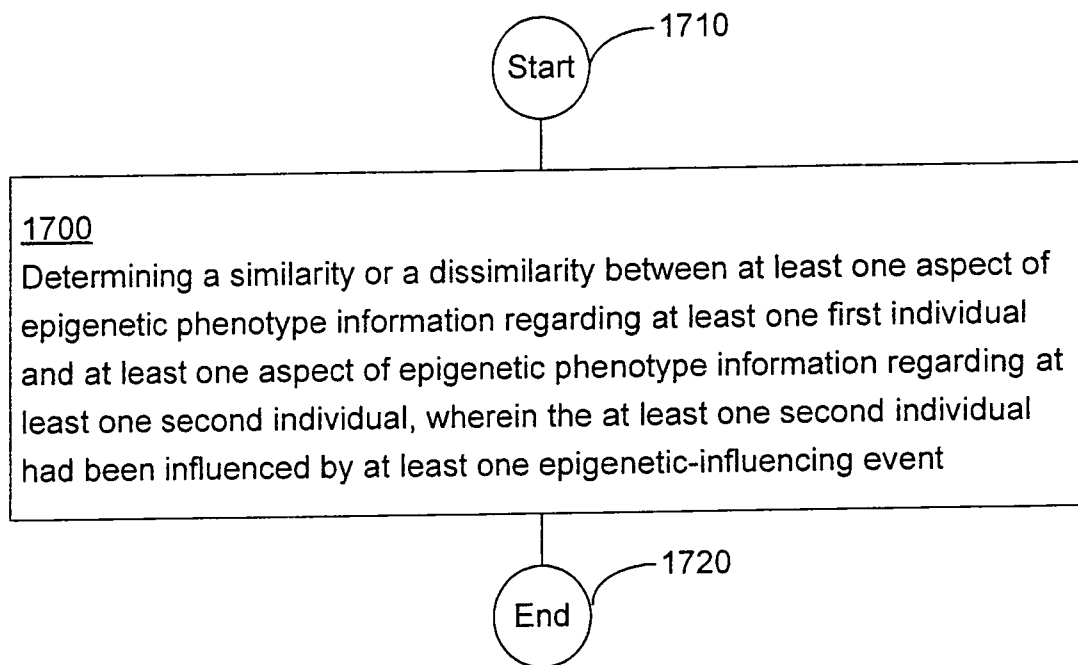


FIG. 18
18/30**1700**

Determining a similarity or a dissimilarity between at least one aspect of epigenetic phenotype information regarding at least one first individual and at least one aspect of epigenetic phenotype information regarding at least one second individual, wherein the at least one second individual had been influenced by at least one epigenetic-influencing event

1800

Wherein the at least one aspect of epigenetic phenotype information regarding at least one first individual comprises at least one aspect of epigenetic phenotype information assayed at more than one time

1810

Wherein the at least one aspect of epigenetic phenotype information regarding at least one first individual includes information regarding DNA methylation

1820

Wherein the at least one aspect of epigenetic phenotype information regarding at least one first individual includes information regarding histone structure

1830

Wherein the at least one aspect of epigenetic phenotype information regarding at least one first individual includes information regarding multiple genomic loci

1840

Wherein the at least one aspect of epigenetic phenotype information regarding at least one first individual includes information regarding mosaicism of at least one first individual

FIG. 19
19/30

1700

Determining a similarity or a dissimilarity between at least one aspect of epigenetic phenotype information regarding at least one first individual and at least one aspect of epigenetic phenotype information regarding at least one second individual, wherein the at least one second individual had been influenced by at least one epigenetic-influencing event

1900

Wherein the at least one aspect of epigenetic phenotype information regarding at least one first individual includes information regarding at least one tissue source

1910

Wherein the information regarding at least one tissue source includes information regarding at least one abnormal tissue source

1920

Wherein the information regarding at least one tissue source includes information regarding at least one type of tissue

1930

Wherein the at least one epigenetic-influencing event includes at least one medical therapy

1940

Wherein the at least one epigenetic-influencing event includes at least one environmental event

FIG. 20
20/30

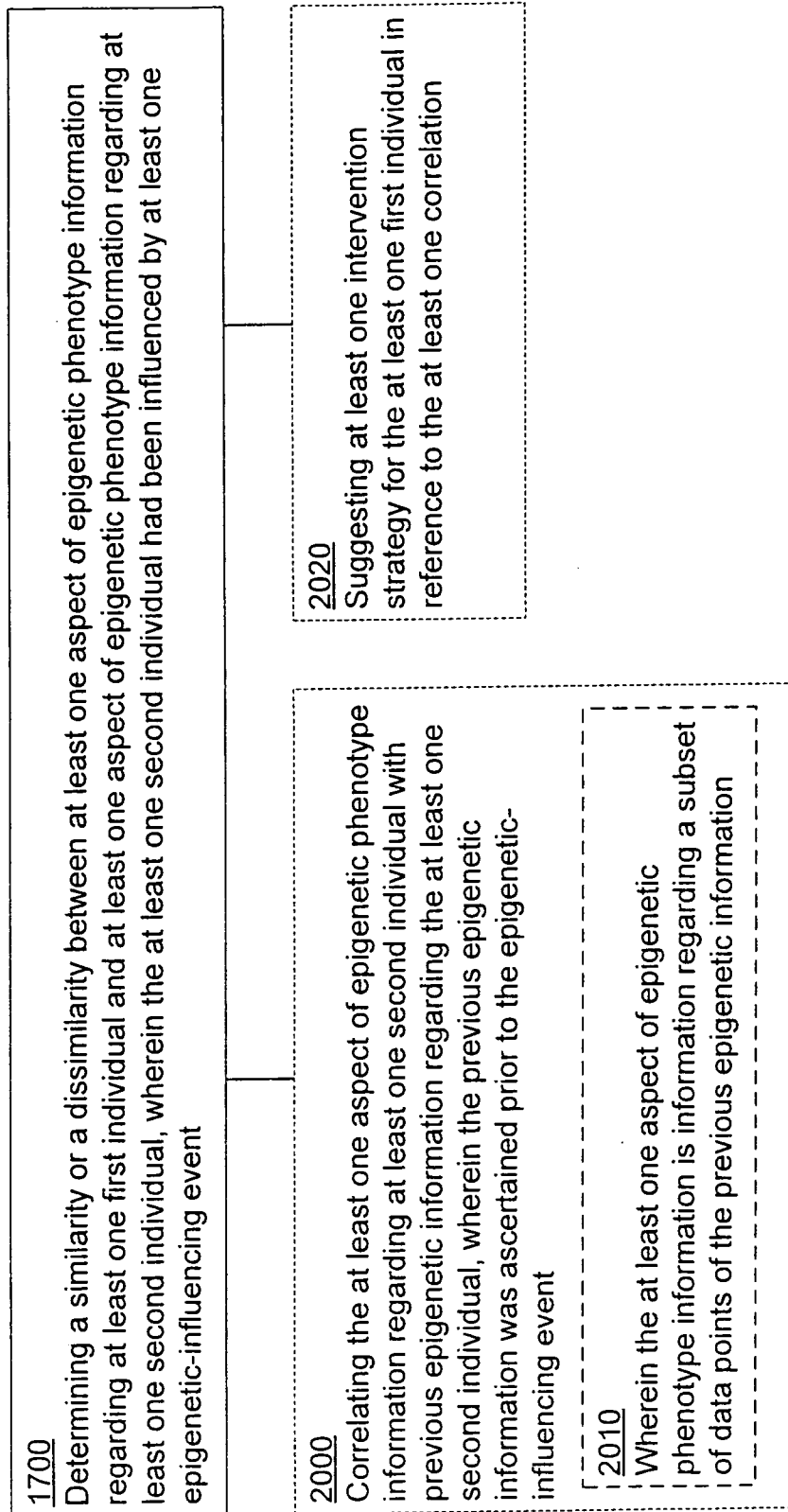


FIG. 21
21/30

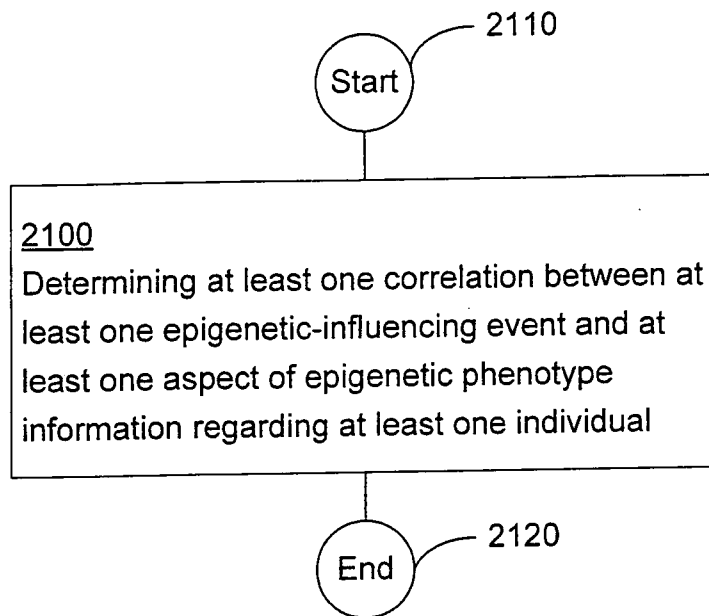


FIG. 22
22/302100

Determining at least one correlation between at least one epigenetic-influencing event and at least one aspect of epigenetic phenotype information regarding at least one individual

2200

Wherein the at least one aspect of epigenetic phenotype information regarding at least one first individual comprises at least one aspect of epigenetic phenotype information assayed at more than one time

2210

Wherein the at least one aspect of epigenetic phenotype information regarding at least one first individual includes information regarding DNA methylation

2220

Wherein the at least one aspect of epigenetic phenotype information regarding at least one first individual includes information regarding histone structure

2230

Wherein the at least one aspect of epigenetic phenotype information regarding at least one first individual includes information regarding multiple genomic loci

2240

Wherein the at least one aspect of epigenetic phenotype information regarding at least one first individual includes information regarding mosaicism of at least one first individual

FIG. 23
23/30

2100

Determining at least one correlation between at least one epigenetic-influencing event and at least one aspect of epigenetic phenotype information regarding at least one individual

2300

Wherein the at least one aspect of epigenetic phenotype information regarding at least one first individual includes information regarding at least one tissue source

2310

Wherein the information regarding at least one tissue source includes information regarding at least one abnormal tissue source

2320

Wherein the information regarding at least one tissue source includes information regarding at least one type of tissue

2330

Wherein the at least one epigenetic-influencing event includes at least one medical therapy

2340

Wherein the at least one epigenetic-influencing event includes at least one environmental event

FIG. 24
24/30

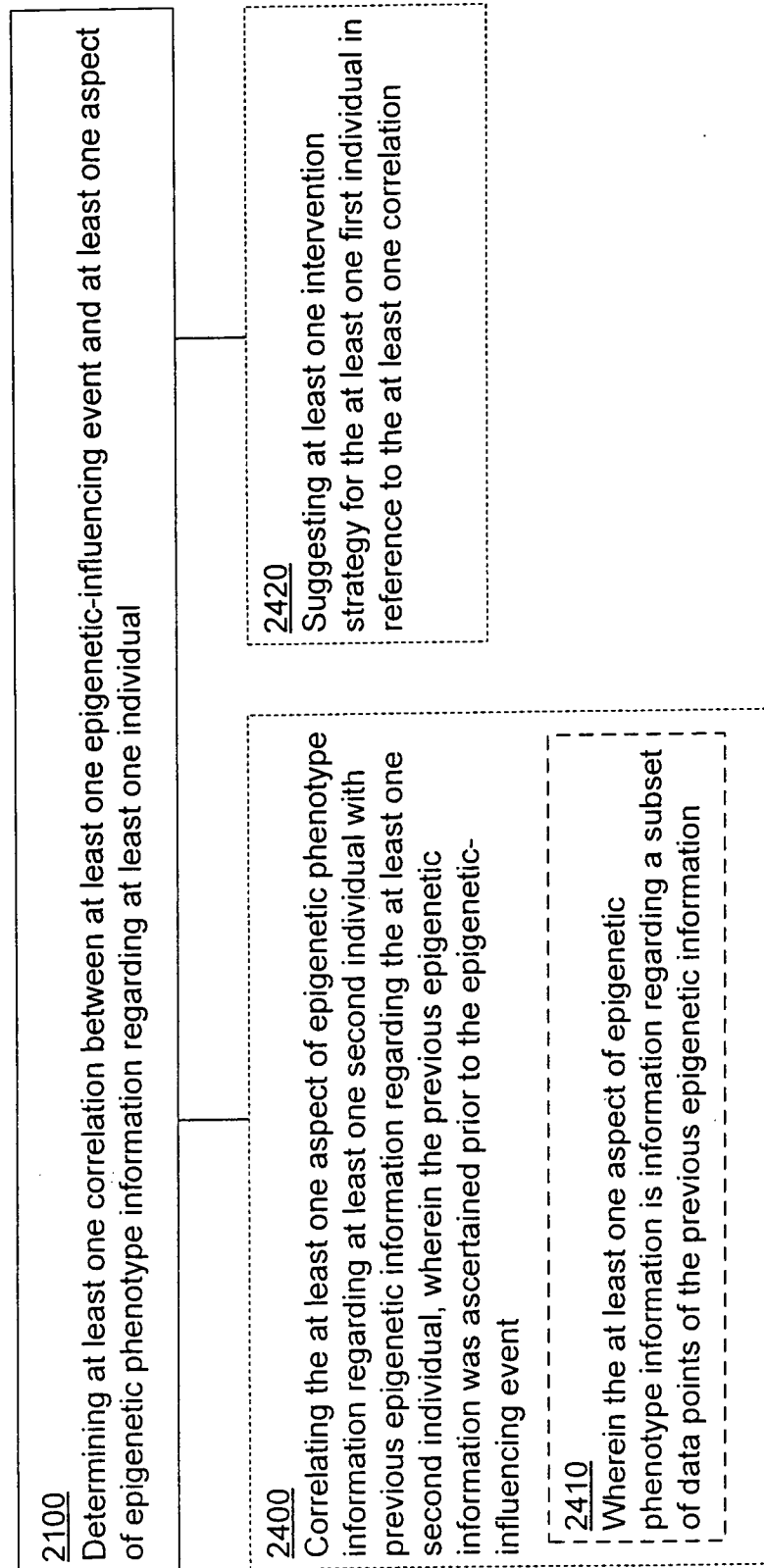


FIG. 25
25/30

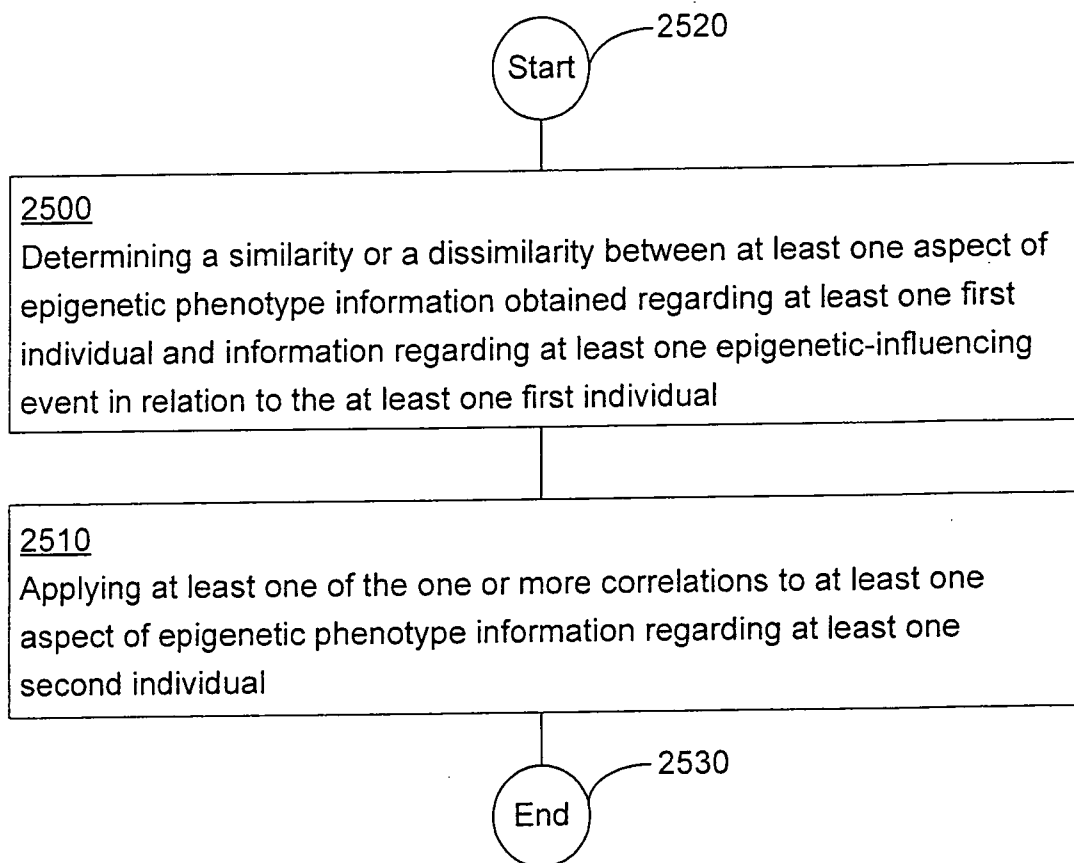


FIG. 26
26/30

2500

Determining a similarity or a dissimilarity between at least one aspect of epigenetic phenotype information obtained regarding at least one first individual and information regarding at least one epigenetic-influencing event in relation to the at least one first individual

2600

Wherein the at least one epigenetic-influencing event includes at least one medical therapy

2610

Wherein the at least one epigenetic-influencing event includes at least one environmental event

2620

Wherein the at least one aspect of epigenetic phenotype information regarding at least one first individual includes information regarding DNA methylation

2630

Wherein the at least one aspect of epigenetic phenotype information regarding at least one first individual includes information regarding at least one tissue source

2510

Applying at least one of the one or more correlations to at least one aspect of epigenetic phenotype information regarding at least one second individual

2640

Predicting at least one epigenetic-influencing event influencing the at least one second individual

2650

Suggesting at least one intervention strategy for one or more of the at least one second individual

FIG. 27
27/30

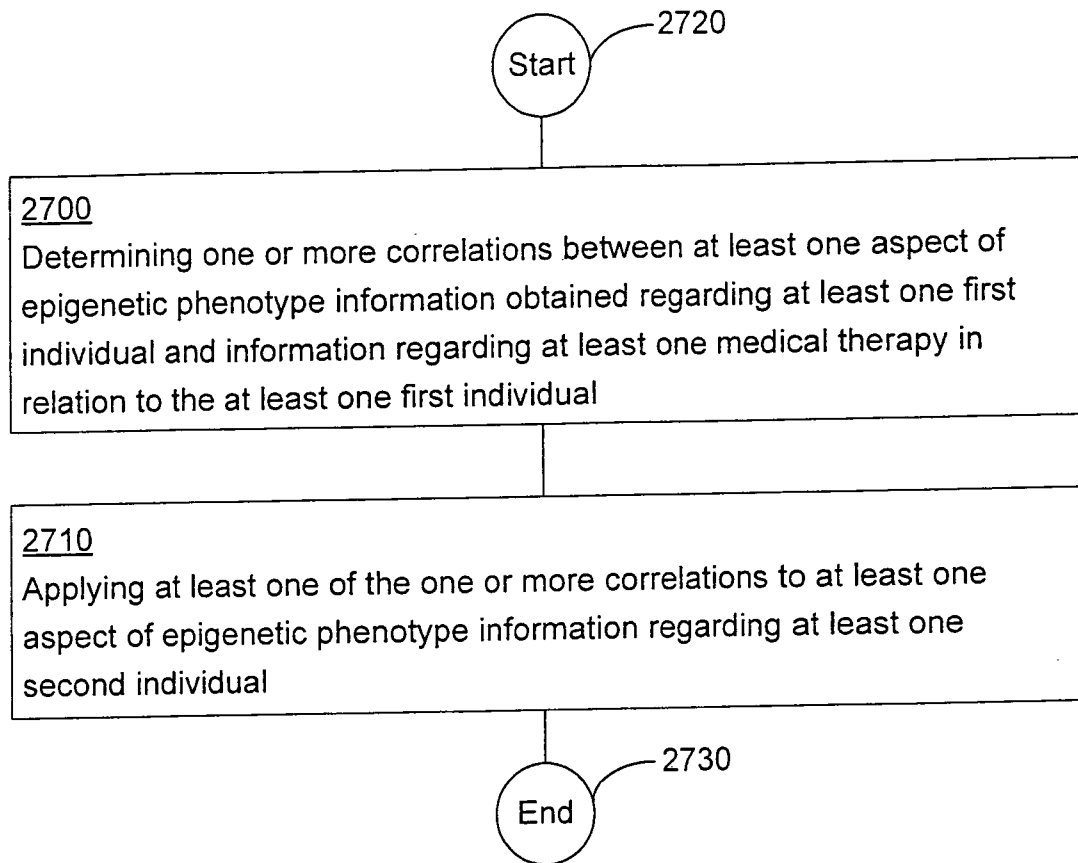


FIG. 28
28/30

2700

Determining one or more correlations between at least one aspect of epigenetic phenotype information obtained regarding at least one first individual and information regarding at least one medical therapy in relation to the at least one first individual

2800

Wherein the at least one medical therapy includes at least one therapeutic agent

2810

Wherein the at least one medical therapy includes at least one energy-based procedure

2820

Wherein the at least one aspect of epigenetic phenotype information regarding at least one first individual includes information regarding DNA methylation

2830

Wherein the at least one aspect of epigenetic phenotype information regarding at least one first individual includes information regarding at least one tissue source

2710

Applying at least one of the one or more correlations to at least one aspect of epigenetic phenotype information regarding at least one second individual

2840

Suggesting at least one intervention strategy for one or more of the at least one second individual

FIG. 29
29/30

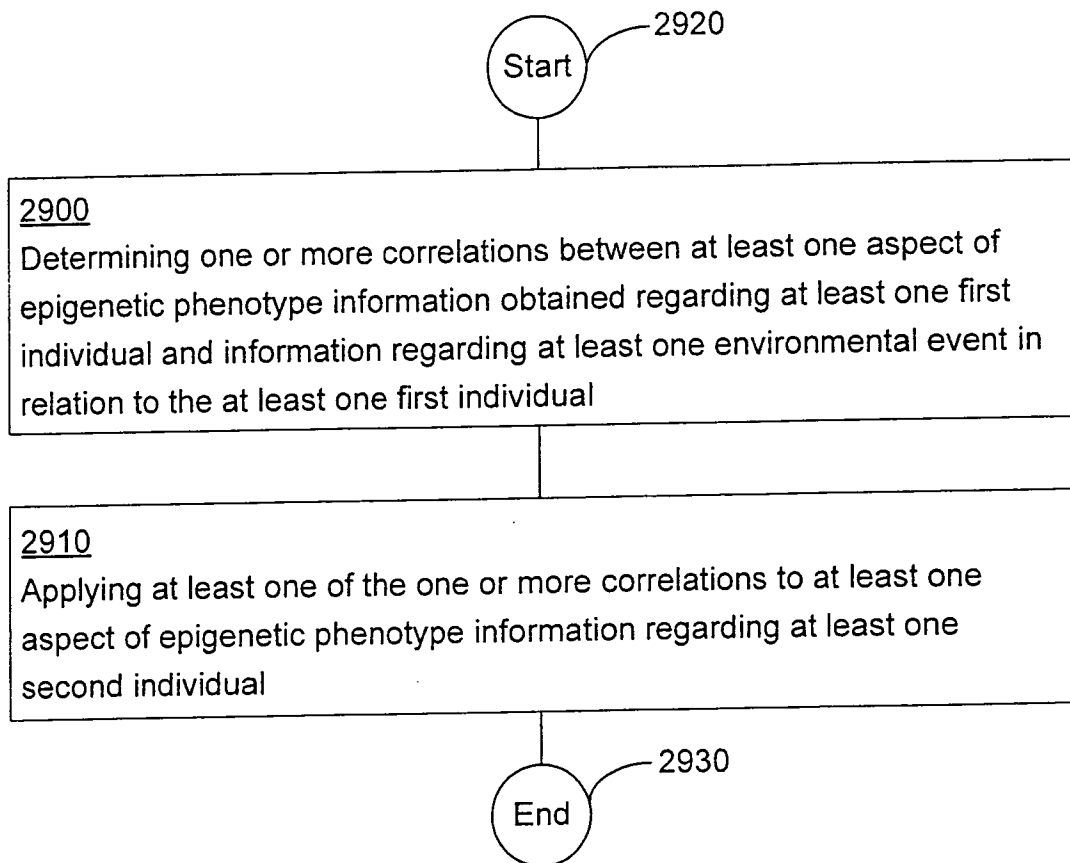


FIG. 30
30/302900

Determining one or more correlations between at least one aspect of epigenetic phenotype information obtained regarding at least one first individual and information regarding at least one environmental event in relation to the at least one first individual

3000

Wherein the at least one environmental event includes at least one environmental pollutant

3010

Wherein the at least one environmental event includes at least one toxin

3020

Wherein the at least one aspect of epigenetic phenotype information regarding at least one first individual includes information regarding DNA methylation

3030

Wherein the at least one aspect of epigenetic phenotype information regarding at least one first individual includes information regarding at least one tissue source

2710

Applying at least one of the one or more correlations to at least one aspect of epigenetic phenotype information regarding at least one second individual

3040

Predicting at least one environmental event influencing the at least one second individual

3050

Suggesting at least one intervention strategy for one or more of the at least one second individual

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 08/08526

A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - G06F 19/00 (2008.04)

USPC - 702/19

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

USPC: 702/19

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
USPC: 702/19 (see also text search)

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

Electronic Databases Searched: PubWEST, USPTO, Google, Answers.com

Search Terms Used: epigenetic, therapy, pollutant, toxin, environment, event, methylation, histone, genomic, loci, mosaicism, tissue, source, abnormal, assay, predict, correlation, influence, medical, computer, data, phenotype, similar, dissimilar

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X ----- Y	US 2006/0292607 A1 (CAPRIOLI et al.) 28 December 2006 (28.12.2006) para [0007], [0017], [0025], [0029], [0033]-[0034], [0037], [0055], [0058], [0062], [0079], [0101] and [0104]	1-6 and 8 ----- 7, 10, 13, 16, 18, 21, 24, 26, 29, 31, 33, 35 and 38
X ----- Y	US 2002/0192686 A1 (ADORJAN et al.) 19 December 2002 (19.12.2002) para [0011], [0013]-[0016], [0021], [0033], [0045], [0064], [0066]-[0067], [0069], [0079], [0084]-[0085], [0088], [0126] and [0128]-[0129]	9, 11-12, 14-15, 17, 19-20, 22-23, 25, 27-28, 30, 32, 34 and 36-37 ----- 7, 10, 13, 16, 18, 21, 24, 26, 29, 31, 33, 35 and 38
A	US 5,416,017 A (BURTON et al.) 16 May 1995 (16.05.1995)	1-38

☐ Further documents are listed in the continuation of Box C.

* Special categories of cited documents:

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"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

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"&" document member of the same patent family

Date of the actual completion of the international search

07 October 2008 (07.10.2008)

Date of mailing of the international search report

24 OCT 2008

Name and mailing address of the ISA/US

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