CLAIMS

1. A method for identifying a modulator of a biological system, said method comprising:

(1) obtaining a first data set representing expression levels of a plurality of genes in cells associated with the biological system;

(2) obtaining a second data set representing a functional activity or a cellular response of the cells associated with the biological system;

(3) generating a first causal relationship network model relating the expression levels of the plurality of genes and the functional activity or cellular response based on the first data set and the second data set using a first programmed computing system, wherein generating the first causal relationship network model comprises:

determining a probabilistic score for each network fragment in a set of network fragments based on the first data set and the second data set;

generating one or more trial networks each constructed from a subset of the network fragments; and

evolving each of the one or more trial networks through local transformations resulting in a consensus relationship network;

(4) generating a differential causal relationship network from the first causal relationship network model and a second causal relationship network model based on control cell data; and

(5) identifying a causal relationship unique in the biological system from the generated differential causal relationship network, wherein a gene associated with the unique causal relationship is identified as a modulator of the biological system.

2. A method for identifying a modulator of a disease process, said method comprising:

(1) obtaining a first data set representing expression levels of a plurality of genes in disease related cells;

(2) obtaining a second data set representing a functional activity or a cellular response of the disease related cells;

(3) generating a first causal relationship network model relating the expression levels of the plurality of genes and the functional activity or cellular response based on the first data set and the second data set using a programmed computing system, wherein generating the first causal relationship network model comprises:

determining a probabilistic score for each network fragment in a set of network fragments based on the first data set and the second data set

generating one or more trial networks each constructed from a subset of the network fragments; and

evolving each of the one or more trial networks through local transformations resulting in a consensus relationship network;

(4) generating a differential causal relationship network from the first causal relationship network model and a second causal relationship network model based on control cell data; and

(5) identifying a causal relationship unique in the disease process from the generated differential causal relationship network, wherein a gene associated with the unique causal relationship is identified as a modulator of the disease process.

3. The method of claim 1, wherein the modulator stimulates or promotes the biological system.

4. The method of claim 1, wherein the modulator inhibits the biological system.

5. The method of claim 2, wherein the disease process is cancer, diabetes, obesity or cardiovascular disease.

6. The method of claim 5, wherein the cancer is lung cancer, breast cancer, prostate cancer, melanoma, squamous cell carcinoma, colorectal cancer, pancreatic cancer, thyroid cancer, endometrial cancer, bladder cancer, kidney cancer, a solid tumor, leukemia, non-Hodgkin lymphoma, or a drug-resistant cancer.

7. The method of claim 2, wherein the modulator stimulates or promotes the disease process.

8. The method of claim 2, wherein the modulator inhibits the disease process.

9. The method of claim 8, wherein the modulator shifts an energy metabolic pathway specifically in disease cells from a glycolytic pathway towards an oxidative phosphorylation pathway.

10. The method of claim 1 or claim 2, wherein the control cell data includes a first control data set representing expression levels of a plurality of genes in control cells and a second control data set representing a functional activity or a cellular response of the control cells.

11. The method of claim 10, further comprising obtaining the first control data set and obtaining the second control data set.

12. The method of claim 10, wherein the method further comprises generating the second causal relationship network model, and wherein the second causal relationship model relates the expression levels of the plurality of genes and the functional activity or cellular response of the control cells based on the first control data set and the second control data set.

13. The method of claim 10, wherein the control cells are in an *in vitro* culture.

14. The method of claim 1, wherein the cells associated with the biological system are in an *in vitro* culture.

15. The method of claim 2, wherein the disease related cells are in an *in vitro* culture.

16. The method of claim 1, wherein the cells associated with the biological system are subject to an environmental perturbation, and control cells, from which the control cell data was obtained, are identical cells not subject to the environmental perturbation.

17. The method of claim 1, wherein the disease related cells are subject to an environmental perturbation, and control cells, from which the control cell data was obtained, are identical cells not subject to the environmental perturbation.

18. The method of claim 16 or 17, wherein the environmental perturbation comprises one or more of a contact with an agent, a change in culture condition, an introduced genetic modification / mutation, and a vehicle that causes a genetic modification / mutation.

19. The method of claim 2, wherein an *in vitro* culture of the disease related cells represents a characteristic aspect of the disease process, and wherein the characteristic aspect of the disease process comprises a hypoxia condition, a hyperglycemic condition, a lactic acid rich culture condition, or a combination thereof.

20. The method of claim 1 or 2, wherein the first data set comprises protein and/or mRNA expression levels of the plurality of genes.

21. The method of claim 1 or 2, wherein the first data set further comprises one or more of lipidomics data, metabolomics data, transcriptomics data, and single nucleotide polymorphism (SNP) data.

22. The method of claim 1 or 2, wherein the second data set comprises data indicative of one or more of bioenergetics profiling, cell proliferation, apoptosis, organellar function, a level of Adenosine Triphosphate (ATP), a level of Reactive Oxygen Species (ROS), a level of Oxidative Phosphorylation (OXPHOS), a level of Oxygen Consumption Rate (OCR), and a level of Extra Cellular Acidification Rate (ECAR).

23. The method of claim 1 or 2, wherein step (3) is carried out by an artificial intelligence (AI)-based informatics platform.

24. The method of claim 23, wherein the AI-based informatics platform is configured to:

(a) create a library of network fragments based on input data via a Bayesian Fragment Enumeration process;

(b) create the one or more trial networks, each trial network constructed from a different subset of the network fragments in the library; and

(c) evolve each of the one or more trial networks through local transformations to produce one or more evolved trial networks that is the consensus relationship network, the AI-based informatics platform including multiple processors for evolution of the one or more trial networks in parallel.

25. The method of claim 23, wherein the AI-based informatics platform receives all data input from the first data set and the second data set without applying a statistical cut-off point.

26. The method of claim 1 or 2, wherein the causal relationship network model is refined by *in silico* simulation based on input data, to provide a confidence level of prediction for one or more causal relationships within the causal relationship network model, and wherein the input data comprises some or all of the data in the first data set and the second data set.

27. The method of any one of claims 1-26, further comprising validating the identified unique causal relationship in a biological system.

28. The method of claim 1 or claim 2, further comprising generating a delta-delta causal relationship network based on the differential causal relationship network and a second differential causal relationship network generated based on data obtained from comparison cells.

29. The method of claim 28, wherein the comparison cells are normal cells.

30. A method for identifying a modulator of a biological system, said method comprising:

(1) generating, using a programmed computing system, a causal relationship network model from a first data set and second data set obtained from a model for the biological system, wherein the model comprises cells associated with the biological system, and wherein the first data set represents expression levels of a plurality of genes in the cells and the second data set represents a functional activity or a cellular response of the cells, and wherein generating the first causal relationship network model comprises:

determining a probabilistic score for each network fragment in a set of network fragments based on the first data set and the second data set

generating one or more trial networks each constructed from a subset of the network fragments; and

evolving each of the one or more trial networks through local transformations resulting in a consensus relationship network;

(2) generating a differential causal relationship network from the first causal relationship network model and a second causal relationship network model based on control cell data; and; and

(3) identifying a causal relationship unique in the biological system from the generated differential causal relationship network, wherein a gene associated with the unique causal relationship is identified as a modulator of the biological system;

thereby identifying a modulator of the biological system.

31. A method for identifying a modulator of a disease process, said method comprising:

(1) generating, using a programmed computing system, a causal relationship network model from a first data set and a second data set obtained from a disease model, wherein the disease model comprises disease related cells, and wherein the first data set represents expression levels of a plurality of genes in the disease related cells and the second data set represents a functional activity or a cellular response of the disease related cells, and wherein generating the first causal relationship network model comprises:

determining a probabilistic score for each network fragment in a set of network fragments based on the first data set and the second data set

generating one or more trial networks each constructed from a subset of the network fragments; and

evolving each of the one or more trial networks through local transformations resulting in a consensus relationship network;

(2) generating a differential causal relationship network from the first causal relationship network model and a second causal relationship network model based on control cell data; and

(3) identifying a causal relationship unique in the disease process from the generated causal relationship network, wherein a gene associated with the unique causal relationship is identified as a modulator of the disease process;

thereby identifying a modulator of the disease process.

32. The method of any one of claims 1, 2, 30 and 31, wherein the probabilistic score determined for each network fragment is a Bayesian probabilistic score; and wherein the generated one or more trial networks is an ensemble of trial networks.

33. The method of claim 32, wherein generating the causal relationship network further comprises:

applying simulated perturbations to each node in the consensus relationship network while observing the effects on other nodes to obtain information regarding directionality of each relationship in the consensus relationship network; and

applying the obtained information regarding directionality of each relationship to the consensus relationship network to obtain the causal relationship network.

34. The method of any one of claims 1, 2, 30 and 31, wherein the causal relationship network and the second causal relationship network each include one or more Bayesian networks.

35. The method of any one of claims 1, 2, 30 and 31, further comprising displaying a graphical representation of the generated differential causal relationship network.

36. The method of any one of claims 1, 2, 30 and 31, further comprising storing a representation of the generated differential causal relationship network.

37. The method of any one of claims 1, 2, 30 and 31, wherein the differential causal relationship network includes:

relationships that are present in the causal relationship network model but absent from the second causal relationship network model, or relationships that are present in the second causal relationship network model but absent from the causal relationship network model; and

relationships having at least one significantly different parameter in the causal relationship network model than in the second causal relationship network model.

38. The method of any one of claims 1, 2, 30 and 31, wherein generating the differential causal relationship network comprises steps including:

i) for each relationship between two nodes in a selected one of the causal relationship network model and the second causal relationship network model, determining if the other causal relationship network model includes a relationship between the same two nodes, and, where the other causal relationship network model includes a relationship between the same two nodes, determining if the relationship between the same two nodes in the other causal relationship network model has at least one significantly different parameter than that of the relationship in the selected causal relationship network model; and

ii) forming the differential causal relationship network including the relationships in the selected causal relationship network model that are absent from the other causal relationship network model and including the relationships in the selected causal relationship network model that have

at least one significantly different parameter in the other causal relationship network model.

39. The method of claim 36 or claim 37, wherein the at least one significantly different parameter is a directionality of the relationship or a quantitative magnitude of the strength of the relationship.

40. The method of any one of claims 1, 2, 30 and 31, wherein the causal relationship network model is generated solely based on the first data set and the second data set and is not generated based on any known relationships other than the first data set and the second data set.