What is claimed is:

1. A method for the diagnosis of a disease comprising:

determining the difference between a basal level or state of a molecule in a sample and the level or state of the molecule after contacting a portion of the sample with a modulator *ex vivo*, wherein the difference is expressed as a value which is indicative of the presence, absence or risk of having a disease.

2. The method of claim 1, wherein the molecule comprises a protein, nucleic acid, lipid, sugar, carbohydrate, or metabolite molecule.

3. The method of claim 1, wherein the sample is selected from the group consisting of tissue, blood, ascites, saliva, urine, perspiration, tears, semen, serum, plasma, amniotic fluid, pleural fluid, cerebrospinal fluid, a cell line, a xenograft, a tumor, pericardial fluid, and combinations thereof.

4. The method of claim 1, wherein the disease is selected from the group consisting of stroke, cardiovascular disease, chronic obstructive pulmonary disorder, myocardial infarction, congestive heart failure, cardiomyopathy, myocarditis, ischemic heart disease, coronary artery disease, cardiogenic shock, vascular shock, pulmonary hypertension, pulmonary edema (including cardiogenic pulmonary edema), cancer, pathogen-mediated disease, pleural effusions, rheumatoid arthritis, diabetic retinopathy, retinitis pigmentosa, and retinopathies, including diabetic retinopathy and retinopathy of prematurity, inflammatory diseases, restenosis, edema (including edema associated with pathologic situations such as cancers and edema induced by medical interventions such as chemotherapy), asthma, acute or adult respiratory distress syndrome (ARDS), lupus, vascular leakage, transplant (such as organ transplant, acute transplant or heterograft or homograft (such as is employed in burn treatment)) rejection; protection from ischemic or reperfusion injury such as ischemic or reperfusion injury incurred during organ transplantation, transplantation tolerance induction; ischemic or reperfusion injury following angioplasty; arthritis (such as rheumatoid arthritis, psoriatic arthritis or osteoarthritis); multiple sclerosis; inflammatory bowel disease, including ulcerative colitis and Crohn's disease; lupus (systemic lupus erythematosis); graft vs. host diseases; T-cell mediated hypersensitivity diseases, including contact hypersensitivity, delayed-type hypersensitivity, and gluten-sensitive enteropathy (Celiac disease); Type 1 diabetes; psoriasis; contact dermatitis (including that due to poison ivy); Hashimoto's

thyroiditis; Sjogren's syndrome; Autoimmune Hyperthyroidism, such as Graves' disease; Addison's disease (autoimmune disease of the adrenal glands); autoimmune polyglandular disease (also known as autoimmune polyglandular syndrome); autoimmune alopecia; pernicious anemia; vitiligo; autoimmune hypopituatarism; Guillain-Barre syndrome; other autoimmune diseases; cancers, including those where kinases such as Src-family kinases are activated or overexpressed, such as colon carcinoma and thymoma, or cancers where kinase activity facilitates tumor growth or survival; glomerulonephritis, serum sickness; uticaria; allergic diseases such as respiratory allergies (asthma, hayfever, allergic rhinitis) or skin allergies; mycosis fungoides; acute inflammatory responses (such as acute or adult respiratory distress syndrome and ischemia/reperfusion injury); dermatomyositis; alopecia areata: chronic actinic dermatitis; eczema; Behcet's disease; Pustulosis palmoplanteris; Pyoderma gangrenum; Sezary's syndrome; atopic dermatitis; systemic schlerosis; morphea; peripheral limb ischemia and ischemic limb disease; bone disease such as osteoporosis, osteomalacia, hyperparathyroidism, Paget's disease, and renal osteodystrophy;vascular leak syndromes, including vascular leak syndromes induced by chemotherapies or immunomodulators such as IL-2; spinal cord and brain injury or trauma; glaucoma; retinal diseases, including macular degeneration; vitreoretinal disease; pancreatitis; vasculatides, including vasculitis, Kawasaki disease, thromboangiitis obliterans, Wegener´s granulomatosis, and Behcet's disease; scleroderma; preeclampsia; thalassemia; Kaposi's sarcoma; and von Hippel Lindau disease.

5. The method of claim 4, wherein the cancer is selected from the group consisting of colorectal, esophageal, stomach, lung, prostate, uterine, breast, skin, endocrine , urinary, pancreas, ovarian, cervical, head and neck, liver, bone, biliary tract, small intestine, hematopoietic, vaginal, testicular, anal, kidney, brain, eye cancer, leukemia, lymphoma, soft tissue, melanoma, and metastases thereof.

6. The method of claim 4, wherein the pathogen is selected from the group consisting of bacteria, fungi, viruses, spirochetes, and parasites.

7. The method of claim 6, wherein the virus is selected from the group consisting of Herpes simplex virus 1 (HSV1), Herpes simplex virus 2 (HSV2), respiratory syncytial virus, measles virus (MV), human cytomegalovirus (HCMV), vaccinia virus, human immunodeficiency virus type 1 (HIV-1), and hepatitis C virus (HCV).

8. The method of claim 3, wherein the tumor sample is from a solid tumor.

9. The method of claim 8, wherein the tumor sample is obtained by fine needle aspiration, core biopsy, circulating tumor cells, or surgically excised tissue sample.

10. The method of claim 2, wherein the protein is modified by post-translational modification.

11. The method of claim 10, wherein the post-translational modification is selected from the group consisting of phosphorylation, acetylation, amidation, methylation, nitrosylation, fatty acid addition, lipid addition, glycosylation, and ubiquitination.

12. The method of claim 1, wherein the modulator is selected from a physical, biological or a chemical modulator.

13. The method of claim 1, further comprising exposing the sample to a therapeutic agent or a combination thereof.

14. The method of claim 1, wherein the determining is with a computer.

15. The method of claim 1, wherein the molecule is analyzed using a method selected from the group consisting of an array, ELISA, bioplex, luminex, mass spectrometry, flow cytometry, PCR and RIA.

16. A method for the prognosis of a disease comprising:

determining the difference between a basal level or state of a molecule in a sample and the level or state of the molecule after contacting a portion of the sample with a modulator *ex vivo*; wherein the difference in the basal level or state of the molecule expressed as a value is indicative of the prognosis.

17. The method of claim 16, wherein the molecule comprises a protein, nucleic acid, lipid, sugar, carbohydrate, or metabolite molecule.

18. The method of claim 16, wherein the sample is selected from the group consisting of tissue, blood, ascites, saliva, urine, perspiration, tears, semen, serum, plasma, amniotic fluid, pleural fluid, cerebrospinal fluid, a cell line, a xenograft, a tumor, pericardial fluid, and combinations thereof.

19. The method of claim 16, wherein the disease is selected from the group consisting of stroke, cardiovascular disease, chronic obstructive pulmonary disorder, myocardial infarction, congestive heart failure, cardiomyopathy, myocarditis, ischemic heart disease, coronary artery disease, cardiogenic shock, vascular shock, pulmonary hypertension, pulmonary edema (including cardiogenic pulmonary edema), cancer, pathogen-mediated disease, pleural effusions, rheumatoid arthritis, diabetic retinopathy, retinitis pigmentosa, and retinopathies, including diabetic retinopathy and retinopathy of prematurity, inflammatory diseases, restenosis, edema (including edema associated with pathologic situations such as cancers and edema induced by medical interventions such as chemotherapy), asthma, acute or adult respiratory distress syndrome (ARDS), lupus, vascular leakage, transplant (such as organ transplant, acute transplant or heterograft or homograft (such as is employed in burn treatment)) rejection; protection from ischemic or reperfusion injury such as ischemic or reperfusion injury incurred during organ transplantation, transplantation tolerance induction; ischemic or reperfusion injury following angioplasty; arthritis (such as rheumatoid arthritis, psoriatic arthritis or osteoarthritis); multiple sclerosis; inflammatory bowel disease, including ulcerative colitis and Crohn's disease; lupus (systemic lupus erythematosis); graft vs. host diseases; T-cell mediated hypersensitivity diseases, including contact hypersensitivity, delayed-type hypersensitivity, and gluten-sensitive enteropathy (Celiac disease); Type 1 diabetes; psoriasis; contact dermatitis (including that due to poison ivy); Hashimoto's thyroiditis; Sjogren's syndrome; Autoimmune Hyperthyroidism, such as Graves' disease; Addison's disease (autoimmune disease of the adrenal glands); autoimmune polyglandular disease (also known as autoimmune polyglandular syndrome); autoimmune alopecia; pernicious anemia; vitiligo; autoimmune hypopituatarism; Guillain-Barre syndrome; other autoimmune diseases; cancers, including those where kinases such as Src-family kinases are activated or overexpressed, such as colon carcinoma and thymoma, or cancers where kinase activity facilitates tumor growth or survival; glomerulonephritis, serum sickness; uticaria; allergic diseases such as respiratory allergies (asthma, hayfever, allergic rhinitis) or skin allergies; mycosis fungoides; acute inflammatory responses (such as acute or adult respiratory distress syndrome and ischemia/reperfusion injury); dermatomyositis; alopecia areata; chronic actinic dermatitis; eczema; Behcet's disease; Pustulosis palmoplanteris; Pyoderma gangrenum; Sezary's syndrome; atopic dermatitis; systemic schlerosis; morphea; peripheral limb ischemia and ischemic limb disease; bone disease such as osteoporosis, osteomalacia, hyperparathyroidism, Paget's disease, and renal osteodystrophy; vascular leak syndromes,

including vascular leak syndromes induced by chemotherapies or immunomodulators such as IL-2; spinal cord and brain injury or trauma; glaucoma; retinal diseases, including macular degeneration; vitreoretinal disease; pancreatitis; vasculatides, including vasculitis, Kawasaki disease, thromboangiitis obliterans, Wegener's granulomatosis, and Behcet's disease; scleroderma; preeclampsia; thalassemia; Kaposi's sarcoma; and von Hippel Lindau disease.

20. The method of claim 19, wherein the cancer is selected from the group consisting of colorectal, esophageal, stomach, lung, prostate, uterine, breast, skin, endocrine , urinary, pancreas, ovarian, cervical, head and neck, liver, bone, biliary tract, small intestine, hematopoietic, vaginal, testicular, anal, kidney, brain, eye cancer, leukemia, lymphoma, soft tissue, melanoma, and metastases thereof.

21. The method of claim 19, wherein the pathogen is selected from the group consisting of bacteria, fungi, viruses, spirochetes, and parasites.

22. The method of claim 21, wherein the virus is selected from the group consisting of Herpes simplex virus 1 (HSV1), Herpes simplex virus 2 (HSV2), respiratory syncytial virus, measles virus (MV), human cytomegalovirus (HCMV), vaccinia virus, human immunodeficiency virus type 1 (HIV-1), and hepatitis C virus (HCV).

23. The method of claim 18, wherein the tumor sample is from a solid tumor.

24. The method of claim 23, wherein the tumor sample is obtained by fine needle aspiration, core biopsy, circulating tumor cells, or surgically excised tissue sample.

25. The method of claim 17, wherein the protein is modified by post-translational modification.

26. The method of claim 25, wherein the post-translational modification is selected from the group consisting of phosphorylation, acetylation, amidation, methylation, nitrosylation, fatty acid addition, lipid addition, glycosylation, and ubiquitination.

27. The method of claim 16, wherein the modulator is selected from a physical, biological or a chemical modulator.

28. The method of claim 16, further comprising exposing the sample to a therapeutic agent or a combination thereof.

29. The method of claim 16, wherein the determining is with a computer.

30. The method of claim 16, wherein the molecule is analyzed using a method selected from the group consisting of an array, ELISA, bioplex, luminex, PCR, mass spectrometry, flow cytometry, and RIA.

31. A method for predicting the effect of an agent comprising:

determining the difference between a basal level or state of a molecule in a sample and the level or state of the molecule after contacting a portion of the sample with a modulator *ex vivo*, wherein the difference in the basal level or state of the molecule expressed as a value is indicative of a positive or negative effect of the agent.

32. The method of claim 31, wherein the agent interacts directly with the molecule in the sample.

33. The method of claim 31, wherein the effect is the activation or inhibition of a cellular pathway selected from the group consisting of a metabolic pathway, a replication pathway, a cellular signaling pathway, an oncogenic signaling pathway, an apoptotic pathway, and a pro-angiogenic pathway.

34. The method of claim 31, wherein the molecule comprises a protein, nucleic acid, lipid, sugar, carbohydrate, or metabolite molecule.

35. The method of claim 31, wherein the sample is selected from the group consisting of tissue, blood, ascites, saliva, urine, perspiration, tears, semen, serum, plasma, amniotic fluid, pleural fluid, cerebrospinal fluid, a cell line, a xenograft, a tumor, pericardial fluid, and combinations thereof.

36. The method of claim 31, wherein the determining is with a computer.

37. The method of claim 31, wherein the molecule is analyzed using a method selected from the group consisting of an array, ELISA, bioplex, luminex, PCR mass spectrometry, flow cytometry, and RIA.

38. A method of monitoring a disease or the course of a subject's therapy comprising:

determining the difference between a basal level or state of a molecule in a sample and the level or state of the molecule after contacting a portion of the sample with a modulator *ex vivo*, optionally prior to, simultaneously with or following a course of therapy; wherein the difference in the basal level or state of the molecule expressed as a value is indicative of a positive or negative treatment.

39. The method of claim 38, wherein a positive treatment is indicative of the subject being a responder to the course of therapy.

40. The method of claim 38, wherein a negative treatment is indicative of the subject having resistance to the course of therapy.

41. A method of screening test agents for an effect on a molecule comprising:

contacting a sample containing the molecule or molecules with the test agent *ex vivo*;

determining a difference between a basal level or state of the molecule in the sample and the level or state of the molecule after contacting a portion of the sample with a modulator *ex vivo*; wherein a difference in the basal level or state of the molecule before and after contacting with the test agent is indicative of an effect on the molecule.

42. The method of claim 41, wherein functional signaling circuitry is assessed to predict the effect of two test agents in combination.

43. The method of claim 41, wherein the sample is selected from the group consisting of tissue, blood, ascites, saliva, urine, perspiration, tears, semen, serum, plasma, amniotic fluid, pleural fluid, cerebrospinal fluid, a cell line, a xenograft, a tumor, pericardial fluid, and combinations thereof.

44. The method of claim 41, wherein the molecule comprises a protein, nucleic acid, lipid, sugar, carbohydrate, or metabolite molecule.

45. The method of claim 41, wherein the molecule activates or inhibits a cellular pathway selected from the group consisting of a metabolic pathway, a replication pathway, a cellular signaling pathway, an oncogenic signaling pathway, an apoptotic pathway, and a pro-angiogenic pathway.

46. The method of claim 41, wherein the test agent is selected from the group consisting of a small molecule chemical, a chemotherapeutic agent, a hormone, a protein, a peptide, a peptidomimetic, a protein, an antibody, a nucleic acid, an RNAi molecule, and an antisense molecule.

47. A method for stratification of patients based on responsiveness to a therapeutic agent or therapeutic regimen comprising:

determining the difference between a basal level or state of a molecule in a sample from a subject and the level or state of the molecule after contacting a portion of the sample with a modulator *ex vivo*; wherein the difference in the basal level or state of the molecule expressed as a value is indicative of a positive or negative response to a therapeutic agent or therapeutic regimen.

48. The method of claim 47, wherein a positive response is indicative of the subject being a responder to the therapeutic agent or therapeutic regimen.

49. The method of claim 47, wherein a negative response is indicative of the subject having resistance to the therapeutic agent or therapeutic regimen.

50. A method of determining drug sensitivity or resistance comprising comparing the basal level or state of a molecule in a sample from a subject with the level or state of the molecule after *ex vivo* inhibition in the absence or presence of a stimulatory compound.

51. The method of claim 50, wherein the molecule comprises a protein, nucleic acid, lipid, sugar, carbohydrate, or metabolite molecule.

52. An *ex vivo* method for determining functional stratification of a live tumor sample of a subject, comprising:

measuring at least one signal transduction phosphoprotein level for creating functional signaling profiles, in the presence of growth factor stimulation and in the absence of growth factor stimulation, and, in the presence of an inhibitor and in the absence of the inhibitor.

53. The method of claim 52, wherein the inhibitor comprises a MEK inhibitor, mTOR inhibitor, BRAF inhibitor, or combinations thereof.

54. The method of claim 52, wherein the live tumor sample comprises breast cancer cells, melanoma cells, or pancreatic cancer cells.

55. The method of claim 52, wherein the phosphoprotein comprises p-Erk 1/2, p-AKT, p-EGFR, p-Stat3, pP70S6K, and/or pGSK3β.

56. The method of claim 52, wherein at least two different groups of functional signaling profiles are identified.

57. The method of claim 52, wherein at least four different groups of functional signaling profiles are identified.

58. The method of claim 52, wherein the growth factor stimulation comprises an Epidermal Growth Factor Receptor ligand.

59. The method of claim 58, wherein the Epidermal Growth Factor Receptor ligand is Epidermal Growth Factor (EGF).

60. A method for classifying cancer cell model systems, comprising:

(a) measuring at least one signal transduction phosphoprotein level to a selected group of cancer cells;

(b) contacting the cancer cells with at least one growth factor or at least one inhibitor;

(c) measuring at least one signal transduction phosphoprotein level after step (b);

(d) calculating a modulation score based on measurements from step (a) and step (c); and

(e) classifying the cancer cells based on the modulation score of step (d).

61. The method of claim 60, further comprising the step of predicting drug resistance or sensitivity of a live tumor sample of a subject based on the classification of the live tumor sample.

62. The method of claim 60, wherein the cancer cells comprise breast cancer cells, melanoma cells, or pancreatic cancer cells.

63. The method of claim 60, wherein the phosphoprotein comprises p-Erk 1/2, p-AKT, p-EGFR, p-Stat3, pP70S6K, and/or pGSK3β.

64. The method of claim 60, wherein at least two different groups of cancer cell classifications are identified.

65. The method of claim 60, wherein at least four different groups of cancer cell classifications are identified.

66. The method of claim 60, wherein the growth factor stimulation comprises an Epidermal Growth Factor Receptor ligand.

67. The method of claim 66, wherein the Epidermal Growth Factor Receptor ligand is Epidermal Growth Factor (EGF).

68. A method for predicting outcome of a therapeutic regimen in a subject comprising:

(a) measuring basal level of at least one molecule of at least one cell from a subject having a disease in need of therapy;

(b) exposing the at least one cell to a modulator *ex vivo*;

(c) measuring level of the at least one signal transduction protein after step (b); and

(d) comparing the difference between levels measured in (a) and (b) to cells with known property for drug resistance or sensitivity, thereby predicting the outcome of the therapeutic regimen in the subject.

69. The method of claim 68, wherein the at least one molecule comprises a signal transduction protein.

70. The method of claim 68, wherein the at least one cell comprises a melanoma cell.

71. The method of claim 68, wherein the drug comprises a MEK inhibitor, mTOR inhibitor, BRAF inhibitor, or combinations thereof.

72. The method of claim 68, wherein the at least one cell comprises a tumor sample from a subject and the levels measured in (a) and (b) are performed *ex vivo*.

73. The method of claim 72, wherein the tumor sample is from a solid tumor.

74. The method of claim 72, wherein the tumor sample comprises cancer selected from the group consisting of colorectal, esophageal, stomach, lung, prostate, uterine, breast, skin, endocrine, urinary, pancreas, ovarian, cervical, head and neck, liver, bone, biliary tract, small intestine, hematopoietic, vaginal, testicular, anal, kidney, brain, eye cancer, leukemia, lymphoma, soft tissue, melanoma, and metastases thereof.

75. The method of claim 68, wherein the drug resistance comprises BRAF inhibitor resistance.

76. The method of claim 71, wherein the at least one cell comprises a serine/threonine-protein kinase B-Raf (BRAF) mutation.

77. The method of claim 76, wherein the at least one melanoma cell comprises a BRAF mutation and Cancer Osaka thyroid oncogene (COT) amplification.

78. The method of claim 76, wherein the BRAF mutation is V600E.

79. The method of claim 68, wherein the modulator is selected from a physical, biological or a chemical modulator.

80. The method of claim 68, wherein the modulator comprises epidermal growth factor (EGF), tissue plasminogen activator (TPA), other growth factors, or a combination thereof.

81. The method of claim 68, wherein the at least one molecule comprises a protein involved in a cellular pathway selected from the group consisting of a metabolic pathway, a replication pathway, a cellular signaling pathway, an oncogenic signaling pathway, an apoptotic pathway, and a pro-angiogenic pathway.

82. The method of claim 68, wherein the at least one molecule comprises a protein involved in RAS-RAF-MEK-ERK pathway.

83. The method of claim 68, wherein the at least one molecule comprises pErk1/2, pAKT, pP70S6k, pGSK3α/β, pEGFR, pSTAT3, or combinations thereof.

84. The method of claim 68, wherein the comparing step is performed with a computer.

85. The method of claim 68, wherein the measurements are performed using an assay selected from the group consisting of an array, ELISA, bioplex, luminex, mass spectrometry, flow cytometry, PCR and RIA.

86. A method for classifying melanoma cells comprising:

(a) measuring a first basal level of at least one molecule of at least one melanoma cell;

(b) comparing the first basal level measured in (a) to a second basal level of the at least one molecule of melanoma cells with known classifications, thereby classifying the at least one melanoma cell.

87. The method of claim 86, wherein the at least one melanoma cell comprises a tumor sample from a subject and the first basal level is measured *ex vivo*.

88. The method of claim 87, wherein the tumor sample comprises cancer selected from the group consisting of colorectal, esophageal, stomach, lung, prostate, uterine, breast, skin, endocrine, urinary, pancreas, ovarian, cervical, head and neck, liver, bone, biliary tract, small intestine, hematopoietic, vaginal, testicular, anal, kidney, brain, eye cancer, leukemia, lymphoma, soft tissue, melanoma, and metastases thereof.

89. The method of claim 86, wherein the at least one molecule comprises a protein involved in a cellular pathway selected from the group consisting of a metabolic pathway, a replication pathway, a cellular signaling pathway, an oncogenic signaling pathway, an apoptotic pathway, and a pro-angiogenic pathway.

90. The method of claim 86, wherein the at least one molecule comprises a protein involved in RAS-RAF-MEK-ERK pathway.

91. The method of claim 86, wherein the at least one molecule comprises pErk1/2, pAKT, pP70S6k, pGSK3α/β, pEGFR, pSTAT3, or combinations thereof.

92. The method of claim 86, wherein the classifications comprise metastatic state.

93. The method of claim 86, wherein the comparing step is performed with a computer.

94. The method of claim 86, wherein the measurements are performed using an assay selected from the group consisting of an array, ELISA, bioplex, luminex, mass spectrometry, flow cytometry, PCR and RIA.

95. A method for classifying melanoma cells comprising:

(a) measuring basal level of at least one molecule of at least one melanoma cell;

(b) exposing the at least one melanoma cell to a inhibitory test agent;

(c) measuring level of the at least one molecule after step (b); and

(d) comparing the difference between levels measured in (a) and (b) to melanoma cells with known classifications, thereby classifying the at least one melanoma cell.

96. The method of claim 95, wherein the at least one melanoma cell comprises a tumor sample from a subject and measurements are performed *ex vivo*.

97. The method of claim 95, wherein the tumor sample comprises cancer selected from the group consisting of colorectal, esophageal, stomach, lung, prostate, uterine, breast, skin, endocrine, urinary, pancreas, ovarian, cervical, head and neck, liver, bone, biliary tract, small intestine, hematopoietic, vaginal, testicular, anal, kidney, brain, eye cancer, leukemia, lymphoma, soft tissue, melanoma, and metastases thereof.

98. The method of claim 95, wherein the at least one molecule comprises a protein involved in a cellular pathway selected from the group consisting of a metabolic pathway, a replication pathway, a cellular signaling pathway, an oncogenic signaling pathway, an apoptotic pathway, and a pro-angiogenic pathway.

99. The method of claim 95, wherein the at least one molecule comprises a protein involved in RAS-RAF-MEK-ERK pathway.

100. The method of claim 95, wherein the at least one molecule comprises pErk1/2, pAKT, pP70S6k, pGSK3α/β, pEGFR, pSTAT3, or combinations thereof.

101. The method of claim 95, wherein the inhibitory test agent comprises a MEK inhibitor, mTOR inhibitor, BRAF inhibitor, or combinations thereof.

102. The method of claim 95, wherein the classifications comprise metastatic state.

103. The method of claim 95, wherein the comparing step is performed with a computer.

104. The method of claim 95, wherein the measurements are performed using an assay selected from the group consisting of an array, ELISA, bioplex, luminex, mass spectrometry, flow cytometry, PCR and RIA.

105. A method for identifying drug resistance mechanisms or oncogene bypass mechanisms of melanoma cells comprising:

(a) exposing at least one melanoma cell to a inhibitory test agent;

(b) measuring reductions of a plural of molecules after exposure of (a), thereby identifying drug resistance mechanisms or oncogene bypass mechanisms.

106. The method of claim 105, wherein the at least one melanoma cell comprises a tumor sample from a subject and measurement are performed *ex vivo*.

107. The method of claim 105, wherein the tumor sample comprises cancer selected from the group consisting of colorectal, esophageal, stomach, lung, prostate, uterine, breast, skin, endocrine, urinary, pancreas, ovarian, cervical, head and neck, liver, bone, biliary tract, small intestine, hematopoietic, vaginal, testicular, anal, kidney, brain, eye cancer, leukemia, lymphoma, soft tissue, melanoma, and metastases thereof.

108. The method of claim 105, wherein the at least one molecule comprises a protein involved in a cellular pathway selected from the group consisting of a metabolic pathway, a replication pathway, a cellular signaling pathway, an oncogenic signaling pathway, an apoptotic pathway, and a pro-angiogenic pathway.

109. The method of claim 105, wherein the at least one molecule comprises a protein involved in RAS-RAF-MEK-ERK pathway.

110. The method of claim 105, wherein the at least one molecule comprises pErk1/2, pAKT, pP70S6k, pGSK3α/β, pEGFR, pSTAT3, or combinations thereof.

111. The method of claim 105, wherein the measurements are performed using an assay selected from the group consisting of an array, ELISA, bioplex, luminex, mass spectrometry, flow cytometry, PCR and RIA.

112. The method of claims 1, 16, 31, 38, 41, 47, or 68, wherein the modulator is an inhibitor.

113. The method of claims 1, 16, 31, 38, 41, 47, or 68 wherein the modulator is a stimulator.

What is claimed is:

1. A method for the diagnosis of a disease comprising:
determining the difference between a basal level or state of a class of proteins in a cell sample and the level or state of the proteins after contacting a portion of the sample with a modulator *ex vivo*, within a cartridge in an automated system to evoke functional signaling profiles wherein the difference is expressed as a value used to create functional signaling profiles that stratify the samples into functional groups which is indicative of the presence, absence or risk of having a disease and wherein the protein is modified by post-translational modification.

2. A method for the prognosis of a disease comprising:
determining the difference between a basal level or state of a class of proteins in a cell sample and the level or state of the proteins after contacting a portion of the sample with a modulator *ex vivo* within a cartridge in an automated system to evoke functional signaling profiles, wherein the difference is expressed as a value used to create functional signaling profiles that stratify the samples into functional groups is indicative of the prognosis and wherein the protein is modified by post-translational modification.

3. The method of claim 1 or 2, wherein the sample is selected from the group consisting of tissue, blood, ascites, saliva, urine, perspiration, tears, semen, serum, plasma, amniotic fluid, pleural fluid, cerebrospinal fluid, a cell line, a xenograft, a tumor, pericardial fluid, and combinations thereof.

4. The method of claim 1 or 2 or 3, wherein the disease is selected from the group consisting of stroke, cardiovascular disease, chronic obstructive pulmonary disorder, myocardial infarction, congestive heart failure, cardiomyopathy, myocarditis, ischemic heart disease, coronary artery disease, cardiogenic shock, vascular shock, pulmonary hypertension, pulmonary edema cardiogenic pulmonary edema, cancer, pathogen-mediated disease, pleural effusions, rheumatoid arthritis, diabetic retinopathy, retinitis pigmentosa, and retinopathies, including diabetic retinopathy and retinopathy of prematurity, inflammatory diseases, restenosis, edema, asthma, acute or adult respiratory distress syndrome (ARDS), lupus, vascular leakage, transplant rejection; protection from ischemic or reperfusion injury; ischemic or reperfusion injury following angioplasty; arthritis; multiple sclerosis; inflammatory bowel disease, ulcerative colitis, Crohn's disease; systemic lupus crythematosis; graft vs. host diseases; T-cell mediated hypersensitivity diseases, contact hypersensitivity, delayed-type hypersensitivity, gluten-sensitive enteropathy, Celiac disease; Type 1 diabetes; psoriasis; contact dermatitis; Hashimoto's thyroiditis; Sjogren's syndrome; Autoimmune Hyperthyroidism, Graves' disease; Addison's disease; autoimmune polyglandular disease; autoimmune alopecia; pernicious anemia; vitiligo; autoimmune hypopituatarism; Guillain- Barre syndrome; autoimmune diseases; cancers, colon carcinoma, thymoma, or cancers where kinase activity facilitates tumor growth or survival; glomerulonephritis, serum sickness; uticaria; allergies, respiratory allergies, asthma, hayfever, allergic rhinitis, skin allergies; mycosis fungoides; acute inflammatory responses, acute or adult respiratory distress syndrome; dermatomyositis; alopecia greata; chronic actinic dermatitis; eczema; Behcet's disease;

Pustulosis palmoplanteris; Pyoderma gangrenum; Sezarys syndrome; atopic dermatitis; systemic schlerosis; morphea; peripheral limb ischemia and ischemic limb disease; bone disease, osteoporosis, osteomalacia, hyperparathyroidism, Paget's disease, renal osteodystrophy; vascular leak syndromes, vascular leak syndromes; spinal cord and brain injury or trauma; glaucoma; retinal diseases, including macular degeneration; vitreoretinal disease; pancreatitis; vasculatides, including vasculitis, Kawasaki disease, thromboangiitis obliterans, Wegener's granulomatosis, and Behcet's disease; scleroderma; preeclampsia; thalassemia; Kaposi's sarcoma; and von Hippel Lindau disease.

5. The method of claim 4, wherein the cancer is selected from the group consisting of colorectal, esophageal, stomach, lung, prostate, uterine, breast, skin, endocrine, urinary, pancreas, ovarian, cervical, head and neck, liver, bone, biliary tract, small intestine, hematopoietic, vaginal, testicular, anal, kidney, brain, eye cancer, leukemia, lymphoma, soft tissue, melanoma, and metastases thereof.

6. The method of claim 4, wherein the pathogen is selected from the group consisting of bacteria, fungi, viruses, spirochetes, and parasites.

7. The method of claim 6, wherein the virus is selected from the group consisting of Herpes simplex virus 1 (HSV1), Herpes simplex virus 2 (HSV2), respiratory syncytial virus, measles virus (MY), human cytomegalovirus (HCMV), vaccinia virus, human immunodeficiency virus type 1 (HIV-1), and hepatitis C virus (HCV).

8. The method of claim 3, wherein the tumor sample is from a solid tumor.

9. The method of claim 8, wherein the tumor sample is obtained by fine needle aspiration, core biopsy, circulating tumor cells, or surgically excised tissue sample.

10. The method of any one of claims 1 to 9, wherein the post-translational modification is selected from the group consisting of phosphorylation, acetylation, amidation, methylation, nitrosylation, fatty acid addition, lipid addition, glycosylation, and ubiquitination.

11. The method of any one of claims 1 to 10, wherein the modulator is selected from a physical, biological or a chemical modulator.

12. The method of any one of claims 1 to 11, further comprising exposing the sample to a therapeutic agent or a combination thereof.

13. The method of any one of claims 1 to 12, wherein the determining is with a computer.

14. The method of any one of claim 1 to 13, wherein the molecule is analyzed using a method selected from the group consisting of an array, ELISA, bioplex, luminex, mass spectrometry, flow cytometry, PCR and RIA.

15. A method of monitoring a disease or the course of a subject's therapy comprising: determining the difference between a basal level or state of a class of proteins in a cell
sample and the level or state of the proteins after contacting a portion of the sample with a modulator *ex vivo* within a cartridge in an automated system to evoke functional signaling profiles prior to, simultaneously with or following a course of therapy; wherein the difference in the basal level or state of the protein is expressed as a value used to create functional signaling profiles that stratify the samples into functional groups is indicative of a positive or negative treatment and wherein the protein is modified by post-translational modification.

16. A method for stratification of patients based on responsiveness to a therapeutic agent or therapeutic regimen comprising:

determining the difference between a basal level or state of a class of proteins in a cell sample from a subject and the level or state of the proteins after contacting a portion of the sample with a modulator *ex vivo* within a cartridge in an automated system to evoke functional signaling profiles, wherein the difference in the basal level or state of the proteins expressed as a value used to create functional signaling profiles that stratify the samples into functional groups is indicative of a positive or negative response to a therapeutic agent or therapeutic regimen and wherein the protein is modified by post-translational modification.

17. The method of claim 15 or 16, wherein a positive treatment is indicative of the subject being a responder to the course of therapy.

18. The method of claim 15 or 16, wherein a negative treatment is indicative of the subject having resistance to the course of therapy.

19. A method for predicting outcome of a therapeutic regimen in a subject comprising:

(a) measuring basal level of at least one protein of at least one cell from a subject having a disease in need of therapy;

(b) exposing the at least one cell to a modulator *ex vivo* within a cartridge in an automated system;

(c) measuring level of the at least one signal transduction protein after step (b) wherein the protein is modified by post-translational modification; and

(d) comparing the difference between levels measured in (a) and (b) to cells with known property for drug resistance or sensitivity, thereby predicting the outcome of the therapeutic regimen in the subject.

20. The method of claim 19, wherein the at least one molecule comprises a signal transduction protein.

21. The method of claim 19 or 20, wherein the at least one cell comprises a melanoma cell.

22. The method of any one of claims 19 to 21, wherein the drug comprises a MEK

inhibitor, mTOR inhibitor, BRAF inhibitor, or combinations thereof.

23. The method of claim 19, wherein the at least one cell comprises a tumor sample from a subject and the levels measured in (a) and (b) are performed *ex vivo*.

24. The method of claim 23, wherein the tumor sample is from a solid tumor.

25. The method of claim 23, wherein the tumor sample comprises cancer selected from the group consisting of colorectal, esophageal, stomach, lung, prostate, uterine, breast, skin, endocrine, urinary, pancreas, ovarian, cervical, head and neck, liver, bone, biliary tract, small intestine, hematopoietic, vaginal, testicular, anal, kidney, brain, eye cancer, leukemia, lymphoma, soft tissue, melanoma, and metastases thereof.

26. The method of claim 19, wherein the drug resistance comprises BRAF inhibitor resistance.

27. The method of claim 22, wherein the at least one cell comprises a serine/threonine- protein kinase B-Raf (BRAF) mutation.

28. The method of claim 27, wherein the at least one melanoma cell comprises a BRAF mutation and Cancer Osaka thyroid oncogene (COT) amplification.

29. The method of claim 27, wherein the BRAF mutation is V600E.

30. The method of claim 19, wherein the modulator is selected from a physical, biological or a chemical modulator.

31. The method of claim 19, wherein the modulator comprises epidermal growth factor (EGF), tissue plasminogen activator (TPA), other growth factors, or a combination thereof.

32. The method of claim 19, wherein the at least one molecule comprises a protein involved in a cellular pathway selected from the group consisting of a metabolic pathway, a replication pathway, a cellular signaling pathway, an oncogenic signaling pathway, an apoptotic pathway, and a pro-angiogenic pathway.

33. The method of claim 19, wherein the at least one molecule comprises a protein involved in RAS-RAF-MEK-ERK pathway.

34. The method of claim 19, wherein the at least one molecule comprises pErkl/2, pAKT, pP70S6k, pGSK3α/β, pEGFR, pSTAT3, or combinations thereof.

35. The method of claim 19, wherein the comparing step is performed with a computer.

36. The method of claim 19, wherein the measurements are performed using an assay selected from the group consisting of an array, ELISA, bioplex, luminex, mass

spectrometry.

37. The method of any one of claims 1 to 36, wherein the modulator is an inhibitor.

38. The method of any one of claims 1 to 36, wherein the modulator is a stimulator.

39. The method of any one of claims 1 to 38, substantially as herein disclosed with reference to the Figures and/or Examples.