CLAIMS

WHAT IS CLAIMED IS:

1. A method for treating a subject having or suspected of having a cancer, comprising administering to said subject a therapeutically effective amount of one or more therapeutic agents that causes a difference in expression or activity of protein kinase, membrane associated tyrosine/threonine 1 (PKMYT1) or WEE1 G2 checkpoint kinase (WEE1) in said subject, thereby treating said subject for said cancer, wherein said cancer is associated with cancerous tissue comprising a cell that has a difference in expression or activity level of Protein Phosphatase 2 (PP2A) or a subunit thereof as compared to a healthy control, or wherein said cancer is associated with cancerous tissue comprising a cell that displays mutations and/or deletions in genes encoding subunits of Protein Phosphatase 2 (PP2A) as compared to a healthy control.

2. The method of claim 1, wherein said cancer is associated with cancerous tissue comprising a cell that has a difference in expression or activity level of Protein Phosphatase 2 (PP2A) or a subunit thereof as compared to a healthy control.

3. The method of claim 2, wherein said difference in expression or activity level is a decrease in expression or activity level.

4. The method of claim 1, wherein said cancer is associated with cancerous tissue comprising a cell that displays mutations and/or deletions in genes encoding subunits of Protein Phosphatase 2 (PP2A) as compared to a healthy control.

5. The method of claim 4, wherein the presence or absence of said mutations and/or deletions is identified by an assay of cells derived from tissue obtained from said subject.

6. The method of claim 5, wherein said assay is a next generation sequencing-based assay.

7. The method of claim 1, wherein said one or more therapeutic agents comprises one or more members selected from the group consisting of a small molecule, a protein, an intrabody, a peptide, a ribonucleic acid (RNA) molecule, and, an endonuclease complex and a deoxyribonucleic acid (DNA) construct.

8. The method of claim 7, wherein said DNA construct comprises an endonuclease gene.

9. The method of claim 8, wherein said endonuclease gene encodes a CRISPR associated (Cas) protein.

10. The method of claim 9, wherein said Cas is Cas9.

11. The method of claim 7, wherein said DNA construct comprises a guide RNA targeting a PKMYT1 gene.

12. The method of claim 7, wherein said endonuclease complex comprises an endonuclease.

13. The method of claim 12, wherein said endonuclease is a CRISPR associated (Cas) protein.

14. The method of claim 7, wherein said small molecule comprises a PKMYT1 inhibitor.

15. The method of claim 14, wherein said PKMYT1 inhibitor comprises 5-((5-methoxy-2-((4-morpholinophenyl)amino)pyrimidin-4-yl)amino)-2-methylphenol, *N*-(2-chloro-6-methylphenyl)-2-((6-(4-(2-hydroxyethyl)piperazin-1-yl)-2-methylpyrimidin-4-yl)amino)thiazole-5-carboxamide (dasatinib), 4-((2,4-dichloro-5-methoxyphenyl)amino)-6-methoxy-7-(3-(4-methylpiperazin-1-yl)propoxy)quinoline-3-carbonitrile (bosutinib), *N*-(5-chlorobenzo[*d*][1,3]dioxol-4-yl)-7-(2-(4-methylpiperazin-1-yl)ethoxy)-5-((tetrahydro-2*H*-pyran-4-yl)oxy)quinazolin-4-amine (saracatinib), (*E*)-*N*-(4-((3-chloro-4-fluorophenyl)amino)-3-cyano-7-ethoxyquinolin-6-yl)-4-(dimethylamino)but-2-enamide (pelitinib), *N*-(3-chlorophenyl)-6,7-dimethoxyquinazolin-4-amine (tyrphostin AG 1478), 6-(2,6-dichlorophenyl)-2-((4-(2-(diethylamino)ethoxy)phenyl)amino)-8-methylpyrido[2,3-*d*]pyrimidin-7(8*H*)-one (PD-0166285), 6-(2,6-dichlorophenyl)-8-methyl-2-((4-morpholinophenyl)amino)pyrido[2,3-*d*]pyrimidin-7(8*H*)-one (PD-173952), 6-(2,6-dichlorophenyl)-8-methyl-2-((3-(methylthio)phenyl)amino)pyrido[2,3-*d*]pyrimidin-7(8*H*)-one (PD-173955), or 6-(2,6-dichlorophenyl)-2-((4-fluoro-3-methylphenyl)amino)-8-methylpyrido[2,3-*d*]pyrimidin-7(8*H*)-one (PD-180970).

16. The method of claim 7, wherein said small molecule comprises a WEE1 inhibitor.

17. The method of claim 16, wherein said WEE1 inhibitor comprises 6-(2,6-dichlorophenyl)-2-((4-(2-(diethylamino)ethoxy)phenyl)amino)-8-methylpyrido[2,3-*d*]pyrimidin-7(8*H*)-one (PD-0166285), 2-allyl-1-(6-(2-hydroxypropan-2-yl)pyridin-2-yl)-6-((4-(4-methylpiperazin-1-yl)phenyl)amino)-1,2-dihydro-3*H*-pyrazolo[3,4-*d*]pyrimidin-3-one (MK-1775), 9-hydroxy-4-phenylpyrrolo[3,4-*c*]carbazole-1,3(2*H*,6*H*)-dione (PD-407824), 6-butyl-4-(2-chlorophenyl)-9-hydroxypyrrolo[3,4-*c*]carbazole-1,3(2*H*,6*H*)-dione, or 6-(2-chloro-6-fluorophenyl)-2-((2,4,4-trimethyl-1,2,3,4-tetrahydroisoquinolin-7-yl)amino)imidazo[1,2-*a*]pyrimido[5,4-*e*]pyrimidin-5(6*H*)-one.

18. The method of claim 1, wherein said PP2A subunit is selected from the group consisting of 65 kDa regulatory subunit A alpha (PPP2R1A), 65 kDa regulatory subunit A beta (PPP2R1B), 55 kDa regulatory subunit B alpha (PPP2R2A), 55 kDa regulatory subunit

B beta (PPP2R2B), 55 kDa regulatory subunit B gamma (PPP2R2C), 55 kDa regulatory subunit B delta (PPP2R2D), 72/130 kDa regulatory subunit B (PPP2R3A), 48 kDa regulatory subunit B (PPP2R3B), regulatory subunit B" subunit gamma (PPP2R3C), regulatory subunit B' (PPP2R4), 56 kDa regulatory subunit alpha (PPP2R5A), 56 kDa regulatory subunit beta (PPP2R5B), 56 kDa regulatory subunit gamma (PPP2R5C), 56 kDa regulatory subunit delta (PPP2R5D), 56 kDa regulatory subunit epsilon (PPP2R5E), catalytic subunit alpha (PPP2CA), and catalytic subunit beta (PPP2CB).

19. The method of claim 18, wherein said PP2A subunit is PPP2R2A.

20. The method of claim 1, further comprising administering to said subject a therapeutically effective amount of one or more therapeutic agents that causes a decrease in expression or activity of PPP2R2A.

21. The method of claim 1, wherein said healthy control is from one or more subjects that do not exhibit said cancer.

22. The method of claim 1, wherein said cancerous tissue is breast tissue, pancreatic tissue, uterine tissue, bladder tissue, colorectal tissue, prostate tissue, liver tissue, or ovarian tissue.

23. The method of claim 22, wherein said cancerous tissue is liver tissue.

24. The method of claim 22, wherein said cancerous tissue is ovarian tissue.

25. A composition for treating a subject having or suspected of having a cancer, comprising a formulation comprising at least one therapeutic agent, wherein said at least one therapeutic agent is present in an amount that is effective to cause a difference in expression or activity of protein kinase, membrane associated tyrosine/threonine 1 (PKMYT1) or WEE1 G2 checkpoint kinase (WEE1) following administration to said subject, and wherein said cancer is associated with cancerous tissue comprising a cell that has a difference in expression or activity level of Protein Phosphatase 2 (PP2A) or a subunit thereof as compared to a healthy control, or wherein said cancer is associated with cancerous tissue comprising a cell that displays mutations and/or deletions in genes encoding subunits of Protein Phosphatase 2 (PP2A) as compared to a healthy control.

26. The composition of claim 25, wherein said cancer is associated with cancerous tissue comprising a cell that has a difference in expression or activity level of Protein Phosphatase 2 (PP2A) or a subunit thereof as compared to a healthy control.

27. The composition of claim 26, wherein said difference in expression or activity level is a decrease in expression or activity level.

28. The composition of claim 25, wherein said cancer is associated with cancerous tissue comprising a cell that displays mutations and/or deletions in genes encoding subunits of Protein Phosphatase 2 (PP2A) as compared to a healthy control.

29. The composition of claim 28, wherein the presence or absence of said mutations and/or deletions is identified by an assay of cells derived from tissue obtained from said subject.

30. The composition of claim 29, wherein said assay is a next generation sequencing-based assay.

31. The composition of claim 25, wherein said at least one therapeutic agent comprises one or more members selected from the group consisting of a small molecule, a protein, an intrabody, a peptide, a ribonucleic acid (RNA) molecule, and, an endonuclease complex and a deoxyribonucleic acid (DNA) construct.

32. The composition of claim 31, wherein said DNA construct comprises an endonuclease gene.

33. The composition of claim 32, wherein said endonuclease gene encodes a CRISPR associated (Cas) protein.

34. The composition of claim 33, wherein said Cas is Cas9.

35. The composition of claim 31, wherein said DNA construct comprises a guide RNA directed to a PKMYT1gene.

36. The composition of claim 31, wherein said endonuclease complex comprises an endonuclease.

37. The composition of claim 36, wherein said endonuclease is a CRISPR associated (Cas) protein.

38. The composition of claim 31, wherein said small molecule comprises a PKMYT1 inhibitor.

39. The composition of claim 38, wherein said PKMYT1 inhibitor comprises 5-((5-methoxy-2-((4-morpholinophenyl)amino)pyrimidin-4-yl)amino)-2-methylphenol, *N*-(2-chloro-6-methylphenyl)-2-((6-(4-(2-hydroxyethyl)piperazin-1-yl)-2-methylpyrimidin-4-yl)amino)thiazole-5-carboxamide (dasatinib), 4-((2,4-dichloro-5-methoxyphenyl)amino)-6-methoxy-7-(3-(4-methylpiperazin-1-yl)propoxy)quinoline-3-carbonitrile (bosutinib), *N*-(5-chlorobenzo[*d*][1,3]dioxol-4-yl)-7-(2-(4-methylpiperazin-1-yl)ethoxy)-5-((tetrahydro-2*H*-pyran-4-yl)oxy)quinazolin-4-amine (saracatinib), (*E*)-*N*-(4-((3-chloro-4-fluorophenyl)amino)-3-cyano-7-ethoxyquinolin-6-yl)-4-(dimethylamino)but-2-enamide (pelitinib), *N*-(3-chlorophenyl)-6,7-dimethoxyquinazolin-4-amine (tyrphostin AG 1478), 6-

(2,6-dichlorophenyl)-2-((4-(2-(diethylamino)ethoxy)phenyl)amino)-8-methylpyrido[2,3-*d*]pyrimidin-7(8*H*)-one (PD-0166285), 6-(2,6-dichlorophenyl)-8-methyl-2-((4-morpholinophenyl)amino)pyrido[2,3-*d*]pyrimidin-7(8*H*)-one (PD-173952), 6-(2,6-dichlorophenyl)-8-methyl-2-((3-(methylthio)phenyl)amino)pyrido[2,3-*d*]pyrimidin-7(8*H*)-one (PD-173955), or 6-(2,6-dichlorophenyl)-2-((4-fluoro-3-methylphenyl)amino)-8-methylpyrido[2,3-*d*]pyrimidin-7(8*H*)-one (PD-180970).

40. The composition of claim 31, wherein said small molecule comprises a WEE1 inhibitor.

41. The composition of claim 40, wherein said WEE1 inhibitor comprises 6-(2,6-dichlorophenyl)-2-((4-(2-(diethylamino)ethoxy)phenyl)amino)-8-methylpyrido[2,3-*d*]pyrimidin-7(8*H*)-one (PD-0166285), 2-allyl-1-(6-(2-hydroxypropan-2-yl)pyridin-2-yl)-6-((4-(4-methylpiperazin-1-yl)phenyl)amino)-1,2-dihydro-3*H*-pyrazolo[3,4-*d*]pyrimidin-3-one (MK-1775), 9-hydroxy-4-phenylpyrrolo[3,4-*c*]carbazole-1,3(2*H*,6*H*)-dione (PD-407824), 6-butyl-4-(2-chlorophenyl)-9-hydroxypyrrolo[3,4-*c*]carbazole-1,3(2*H*,6*H*)-dione, or 6-(2-chloro-6-fluorophenyl)-2-((2,4,4-trimethyl-1,2,3,4-tetrahydroisoquinolin-7-yl)amino)imidazo[1,2-*a*]pyrimido[5,4-*e*]pyrimidin-5(6*H*)-one.

42. The composition of claim 25, wherein said PP2A subunit is selected from the group consisting of 65 kDa regulatory subunit A alpha (PPP2R1A), 65 kDa regulatory subunit A beta (PPP2R1B), 55 kDa regulatory subunit B alpha (PPP2R2A), 55 kDa regulatory subunit B beta (PPP2R2B), 55 kDa regulatory subunit B gamma (PPP2R2C), 55 kDa regulatory subunit B delta (PPP2R2D), 72/130 kDa regulatory subunit B (PPP2R3A), 48 kDa regulatory subunit B (PPP2R3B), regulatory subunit B" subunit gamma (PPP2R3C), regulatory subunit B' (PPP2R4), 56 kDa regulatory subunit alpha (PPP2R5A), 56 kDa regulatory subunit beta (PPP2R5B), 56 kDa regulatory subunit gamma (PPP2R5C), 56 kDa regulatory subunit delta (PPP2R5D), 56 kDa regulatory subunit epsilon (PPP2R5E), catalytic subunit alpha (PPP2CA), and catalytic subunit beta (PPP2CB).

43. The composition of claim 42, wherein said PP2A subunit is PPP2R2A.

44. The composition of claim 25, wherein said composition further comprises a formulation comprising at least one therapeutic agent present in an amount that is effective to cause a decrease in expression or activity of PPP2R2A.

45. The composition of claim 25, wherein said healthy control is from one or more subjects that do not exhibit said cancer.

46. The composition of claim 25, wherein said cancerous tissue is breast tissue.

47. The composition of claim 25, wherein said cancerous tissue is liver tissue.

48. The composition of claim 25, wherein said cancerous tissue is ovarian tissue.

49. The composition of claim 25, wherein said formulation further comprises an excipient.

50. The composition of claim 49, wherein said excipient stabilizes said at least one therapeutic agent or provides therapeutic enhancement of said at least one therapeutic agent following administration to said subject as compared to said at least one therapeutic agent being administered to said subject in absence of said excipient.

51. A kit for treating a subject having or suspected of having a cancer, comprising:

a composition comprising a formulation comprising at least one therapeutic agent, wherein said at least one therapeutic agent is present in an amount that is effective to cause a difference in expression or activity of protein kinase, membrane associated tyrosine/threonine 1 (PKMYT1) or WEE1 G2 checkpoint kinase (WEE1) following administration to said subject, and wherein said cancer is associated with cancerous tissue comprising a cell that has a difference in expression or activity level of Protein Phosphatase 2 (PP2A) or a subunit thereof as compared to a healthy control, or wherein said cancer is associated with cancerous tissue comprising a cell that displays mutations and/or deletions in genes encoding subunits of Protein Phosphatase 2 (PP2A) as compared to a healthy control; and

one or more instructions for administration of said composition to said subject.

52. The kit of claim 51, wherein said cancer is associated with cancerous tissue comprising a cell that has a difference in expression or activity level of Protein Phosphatase 2 (PP2A) or a subunit thereof as compared to a healthy control

53. The kit of claim 52, wherein said difference in expression or activity level is a decrease in expression or activity level.

54. The kit of claim 51, wherein said cancer is associated with cancerous tissue comprising a cell that displays mutations and/or deletions in genes encoding subunits of Protein Phosphatase 2 (PP2A) as compared to a healthy control.

55. The kit of claim 54, wherein the presence or absence of said mutations and/or deletions is identified by an assay of cells derived from tissue obtained from said subject.

56. The kit of claim 55, wherein said assay is a next generation sequencing-based assay.

57. A method for identifying a disease in a subject, comprising assaying cells derived from tissue obtained from a subject to identify the presence or absence of mutations and/or deletions in genes encoding subunits of Protein Phosphatase 2 (PP2A) as compared to a healthy control, and outputting a report indicative of the presence or absence of mutations

and/or deletions in genes encoding subunits of Protein Phosphatase 2 (PP2A) as compared to a healthy control.

58. The method of claim 57, wherein said method comprises a next generation sequencing-based assay.

CLAIMS

WHAT IS CLAIMED IS:

1. Use of a therapeutic agent that causes a difference in expression or activity of protein kinase, membrane associated tyrosine/threonine 1 (PKMYT1) or WEE1 G2 checkpoint kinase (WEE1), in the manufacture of a medicament for treating cancer in a subject having or suspecting of having said cancer, wherein said cancer comprises a cell comprising a difference in expression or activity of Protein Phosphatase 2 (PP2A) or a PP2A subunit, or comprises a mutation or deletion of a nucleic acid encoding said PP2A subunit as compared to a non-cancer control; and wherein a therapeutically effective amount of the therapeutic agent is to be administered to the subject.

2. The use of claim 1, wherein said cell comprises said difference in expression or activity of Protein Phosphatase 2 (PP2A) or said PP2A subunit.

3. The use of claim 2, wherein said difference in expression or activity of PP2A or said subunit comprises a decrease in said expression or activity.

4. The use of claim 1, wherein said cell comprises said mutation or deletion of said nucleic acid encoding said PP2A subunit.

5. The use of claim 1, further comprising identifying said cancer as comprising said cell comprising said difference in expression or activity of PP2A or said PP2A submit, or as comprising said mutation or deletion of said nucleic acid encoding said PP2A subunit.

6. The use of claim 1, wherein said therapeutic agent comprises a small molecule, a protein, or a nucleic acid.

7. The use of claim 6, wherein said therapeutic agent comprises a small molecule.

8. The use of claim 7, wherein said small molecule comprises a PKMYT1 inhibitor.

9. The use of claim 8, wherein said PKMYT1 inhibitor comprises 5-((5-methoxy-2-((4-morpholinophenyl)amino)pyrimidin-4-yl)amino)-2-methylphenol, *N*-(2-chloro-6-methylphenyl)-2-((6-(4-(2-hydroxyethyl)piperazin-1-yl)-2-methylpyrimidin-4-yl)amino)thiazole-5-carboxamide (dasatinib), 4-((2,4-dichloro-5-methoxyphenyl)amino)-6-methoxy-7-(3-(4-methylpiperazin-1-yl)propoxy)quinoline-3-carbonitrile (bosutinib), *N*-(5-chlorobenzo[*d*][1,3]dioxol-4-yl)-7-(2-(4-methylpiperazin-1-yl)ethoxy)-5-((tetrahydro-2*H*-pyran-4-yl)oxy)quinazolin-4-amine (saracatinib), (*E*)-*N*-(4-((3-chloro-4-fluorophenyl)amino)-3-cyano-7-ethoxyquinolin-6-yl)-4-(dimethylamino)but-2-enamide (pelitinib), *N*-(3-chlorophenyl)-6,7-dimethoxyquinazolin-4-amine (tyrphostin AG 1478), 6-

(2,6-dichlorophenyl)-2-((4-(2-(diethylamino)ethoxy)phenyl)amino)-8-methylpyrido[2,3-*d*]pyrimidin-7(8*H*)-one (PD-0166285), 6-(2,6-dichlorophenyl)-8-methyl-2-((4-morpholinophenyl)amino)pyrido[2,3-*d*]pyrimidin-7(8*H*)-one (PD-173952), 6-(2,6-dichlorophenyl)-8-methyl-2-((3-(methylthio)phenyl)amino)pyrido[2,3-*d*]pyrimidin-7(8*H*)-one (PD-173955), or 6-(2,6-dichlorophenyl)-2-((4-fluoro-3-methylphenyl)amino)-8-methylpyrido[2,3-*d*]pyrimidin-7(8*H*)-one (PD-180970).

10. The use of claim 7, wherein said small molecule comprises a WEE1 inhibitor.

11. The use of claim 10, wherein said WEE1 inhibitor comprises 6-(2,6-dichlorophenyl)-2-((4-(2-(diethylamino)ethoxy)phenyl)amino)-8-methylpyrido[2,3-*d*]pyrimidin-7(8*H*)-one (PD-0166285), 2-allyl-1-(6-(2-hydroxypropan-2-yl)pyridin-2-yl)-6-((4-(4-methylpiperazin-1-yl)phenyl)amino)-1,2-dihydro-3*H*-pyrazolo[3,4-*d*]pyrimidin-3-one (MK-1775), 9-hydroxy-4-phenylpyrrolo[3,4-*c*]carbazole-1,3(2*H*,6*H*)-dione (PD-407824), 6-butyl-4-(2-chlorophenyl)-9-hydroxypyrrolo[3,4-*c*]carbazole-1,3(2*H*,6*H*)-dione, or 6-(2-chloro-6-fluorophenyl)-2-((2,4,4-trimethyl-1,2,3,4-tetrahydroisoquinolin-7-yl)amino)imidazo[1,2-*a*]pyrimido[5,4-*e*]pyrimidin-5(6*H*)-one.

12. The use of claim 1, wherein said cell comprises said difference in expression or activity of said PP2A subunit, or comprises said mutation or deletion of said nucleic encoding said PP2A; and

wherein said PP2A subunit is selected from the group consisting of 65 kDa regulatory subunit A alpha (PPP2R1A), 65 kDa regulatory subunit A beta (PPP2R1B), 55 kDa regulatory subunit B alpha (PPP2R2A), 55 kDa regulatory subunit B beta (PPP2R2B), 55 kDa regulatory subunit B gamma (PPP2R2C), 55 kDa regulatory subunit B delta (PPP2R2D), 72/130 kDa regulatory subunit B (PPP2R3A), 48 kDa regulatory subunit B (PPP2R3B), regulatory subunit B" subunit gamma (PPP2R3C), regulatory subunit B' (PPP2R4), 56 kDa regulatory subunit alpha (PPP2R5A), 56 kDa regulatory subunit beta (PPP2R5B), 56 kDa regulatory subunit gamma (PPP2R5C), 56 kDa regulatory subunit delta (PPP2R5D), 56 kDa regulatory subunit epsilon (PPP2R5E), catalytic subunit alpha (PPP2CA), and catalytic subunit beta (PPP2CB).

13. The use of claim 12, wherein said PP2A subunit comprises PPP2R1A.

14. The use of claim 12, wherein said PP2A subunit comprises PPP2R2A.

15. The use of claim 1, wherein a therapeutically effective amount of a second therapeutic agent comprising an anti-cancer agent is to be further administered to said subject.

16. The use of claim 1, wherein said cancer comprises a cancerous tissue comprising said cell.

17. The use of claim 16, wherein said cancerous tissue comprises breast tissue, pancreatic tissue, uterine tissue, bladder tissue, colorectal tissue, prostate tissue, liver tissue, or ovarian tissue.

18. The use of claim 16, wherein said cancerous tissue is liver tissue.

19. The use of claim 16, wherein said cancerous tissue is ovarian tissue.

20. The use of claim 1, wherein said subject has said cancer, and said administration reduces proliferation or viability of said cancer.