We claim:

1. Use of a glycine cleavage system (GCS) inhibitor in the manufacture of a medicament for inhibiting the proliferation or survival of a tumor or tumor cell identified as overexpressing serine hydroxymethyltransferase 2 (SHMT2) as compared to a control tissue or cell.

2. Use of a glycine cleavage system (GCS) inhibitor in the manufacture of a medicament for treating a tumor or tumor cell identified as overexpressing serine hydroxymethyltransferase 2 (SHMT2) as compared to a control tissue or cell.

3. The use of claim 1 or 2, wherein the tumor cell is a brain tumor cell, bladder tumor cell, breast tumor cell, cervical tumor cell, colorectal tumor cell, embryonal tumor cell, gastric tumor cell, germ cell tumor cell, head and neck tumor cell, hematologic tumor cell, kidney tumor cell, melanoma cell, mesothelial tumor cell, ovarian tumor cell, yolk sac tumor cell, or sarcoma cell.

4. The use of claim 1 or 2, wherein the tumor is a brain tumor, bladder tumor, breast tumor, cervical tumor, colorectal tumor, embryonal tumor, gastric tumor, germ cell tumor, head and neck tumor, hematologic tumor, kidney tumor, melanoma, mesothelial tumor, ovarian tumor, yolk sac tumor, or sarcoma.

5. The use of claim 1 or 2, wherein the tumor or tumor cell is a glioblastoma muitiforme (GBM) or GBM cell.

6. The use of claim 1 or 2, wherein the tumor or tumor cell is a cancer in which SHMT2 is within the top 1% of overexpressed genes in the cancer.

7. The use of any one of claims 1 to 6, wherein the tumor cell is a tumor stem cell or a human tumor cell.

8. The use of any one of claims 1 to 7, wherein the GCS inhibitor comprises a small molecule; an RNAi agent; or cysteamine or a salt, analog, or prodrug thereof.

9. The use of claim 8, wherein the GCS inhibitor is a glycine dehydrogenase (GLDC) inhibitor or a glycine cleavage system protein H (GCSH) inhibitor.

10. The use of claim 1 or 2, wherein identifying the tumor or tumor cell as overexpressing SHMT2 is determined by measuring *in vitro* SHMT2 polypeptide levels or SHMT2 activity in the tumor or tumor cell.

11. The use of claim 10, wherein measuring SHMT2 polypeptide levels is by immunohistochemistry (IHC).

12. The use of claim 1 or 2, wherein identifying the tumor or tumor cell as overexpressing SHMT2 is determined by measuring *in vitro* SHMT2 mRNA levels in the tumor or tumor cell.

13. The use of claim 1 or 2, wherein identifying the tumor or tumor cell as overexpressing SHMT2 is determined by measuring *in vitro* copy number of a chromosomal region containing at least a portion of the SHMT2 gene in the tumor or tumor cell.

14. The use of claim 1 or 2, wherein identifying the tumor or tumor cell as overexpressing SHMT2 is determined by microarray-based meta-analyses.

15. The use of any one of claims 10 to 14, wherein the measuring of SHMT2 level is determined for a sample containing the tumor or tumor cell.

16. The use of any one of claims 1 to 15, wherein the control is a normal tissue or normal cell.

17. The use of any one of claims 1 to 15, wherein the control is a tumor or tumor cell insensitive to GCS inhibitor.

18. A method for assessing sensitivity of a tumor or tumor cell to a GCS inhibitor, the method comprising: measuring *in vitro* the expression level of serine hydroxymethyltransferase 2 (SHMT2) in a tumor or tumor cell, and comparing the measured level to expression level in a control tissue or cell, wherein an increased expression of SHMT2 as compared to the control

tissue or cell identifies the tumor or tumor cell as having an increased likelihood of sensitivity to the GCS inhibitor.

19. The method of claim 18, wherein the expression level of SHMT2 is determined by measuring *in vitro* SHMT2 polypeptide levels or SHMT2 activity in the tumor or tumor cell.

20. The method of claim 19, wherein measuring SHMT2 polypeptide levels is by immunohistochemistry (IHC).

21. The method of claim 18, wherein the expression of SHMT2 is determined by measuring *in vitro* SHMT2 mRNA level in the tumor or tumor cell.

22. The method of claim 18, wherein the expression level of SHMT2 is determined by measuring *in vitro* copy number of a chromosomal region containing at least a portion of the SHMT2 gene in the tumor or tumor cell.

23. The method of claim 18, wherein the expression level of SHMT2 is determined by microarray-based meta-analyses.

24. The method of any one of claims 18 to 23, wherein the measuring of SHMT2 level is determined for a sample containing the tumor or tumor cell.

25. The method of any one of claims 18 to 24, wherein the control level of SHMT2 is a level in non-tumor tissue or non-tumor cells.

26. The method of any one of claims 18 to 24, wherein the control level of SHMT2 is a level in tumor or tumor cell which is insensitive to the GCS inhibitor.

27. The method of any one of claims 18 to 26, wherein the tumor is a brain tumor, bladder tumor, breast tumor, cervical tumor, colorectal tumor, embryonal tumor, gastric tumor, germ cell tumor, head and neck tumor, hematologic tumor, kidney tumor, melanoma, mesothelial tumor, ovarian tumor, yolk sac tumor, or sarcoma.

28. A method of identifying an anti-tumor agent, the method comprising:

contacting *in vitro* a tumor cell or tumor with a candidate anti-tumor test agent, wherein

the tumor cell or tumor has been identified as overexpressing serine hydroxymethyltransferase 2 (SHMT2), and

determining whether survival, proliferation, growth, maintenance, or metastasis of the tumor cell or tumor is inhibited.

29. The method of claim 28, further comprising determining whether the test agent is an inhibitor of GCS.

30. The method of claim 29, comprising determining whether the test agent inhibits GLDC.

31. The method of claim 29, comprising determining whether the test agent inhibits GCSH.

32. The method of any one of claims 28 to 31, wherein the test agent is an antibody, RNAi or small molecule.

33. The method of any one of claims 28 to 32, wherein the tumor cell is a brain tumor cell, bladder tumor cell, breast tumor cell, cervical tumor cell, colorectal tumor cell, embryonal tumor cell, gastric tumor cell, germ cell tumor cell, head and neck tumor cell, hematologic tumor cell, kidney tumor cell, melanoma cell, mesothelial tumor cell, ovarian tumor cell, yolk sac tumor cell, or sarcoma.

34. An anti-tumor agent identified by the method of any one of claims 28 to 33.

We claim:

1. An *in vitro* method of inhibiting proliferation or survival of a tumor cell, the method comprising contacting the cell with an inhibitor of the glycine cleavage system (GCS).

2. The method of claim 1, wherein the tumor cell overexpresses serine hydroxymethyltransferase 2 (SHMT2) as compared with a control cell.

3. The method of claim 1, wherein the tumor cell is a brain tumor cell, bladder tumor cell, breast tumor cell, cervical tumor cell, colorectal tumor cell, embryonal tumor cell, gastric tumor cell, germ cell tumor cell, head and neck tumor cell, hematologic tumor cell, kidney tumor cell, melanoma cell, mesothelial tumor cell, ovarian tumor cell, yolk sac tumor cell, or sarcoma cell.

4. The method of claim 1, wherein the tumor cell is a glioblastoma multiforme (GBM) cell.

5. The method of claim 1, wherein the tumor cell is a tumor stem cell.

6. The method of claim 1, wherein the tumor cell is a human tumor cell.

7. The method of claim 1, wherein the GCS inhibitor comprises a small molecule.

8. The method of claim 1, wherein the GCS inhibitor comprises an RNAi agent.

9. The method of claim 1, wherein the GCS inhibitor comprises cysteamine or a cysteamine salt, analog, or prodrug.

10. The method of claim 1, wherein the GCS inhibitor is a glycine dehydrogenase (GLDC) inhibitor.

11. The method of claim 1, wherein the GCS inhibitor is a glycine cleavage system protein H (GCSH) inhibitor.

12. The method of claim 1, wherein the tumor cell is in a subject.

13. An *in vitro* method of inhibiting proliferation or survival of a cell that overexpresses SHMT2, the method comprising contacting the cell with an inhibitor of the GCS.

14. The method of claim 13, wherein the cell is a tumor cell.

15. A method of identifying a candidate anti-tumor agent, the method comprising determining whether a test agent binds to or inhibits a GCS component or inhibits the GCS, wherein if the test agent binds to or inhibits a GCS component or inhibits the GCS, the test agent is identified as a candidate anti-tumor agent.

16. The method of claim 15, wherein the method comprises (a) providing one or more GCS components; (b) providing a test agent; and (c) determining whether the test agent binds to or inhibits one or more of the GCS components.

17. The method of claim 16, wherein the GCS component is a recombinantly produced polypeptide.

18. The method of claim 15, wherein the test agent is a small molecule.

19. The method of claim 15, wherein the method comprises high throughput screening.

20. The method of claim 15, wherein the method comprises testing at least 1,000 test agents.

21. The method of claim 15, wherein the method comprises determining whether the test agent inhibits enzymatic activity of a GCS component.

22. The method of claim 15, wherein the method comprises determining whether the test agent binds to or inhibits GLDC.

23. The method of claim 15, wherein the method comprises determining whether the test agent binds to or inhibits GCSH.

24. The method of claim 15, further comprising determining whether the test agent inhibits proliferation or survival of tumor cells or inhibits tumor maintenance, growth, or metastasis.

25. The method of claim 15, further comprising determining whether the test agent inhibits proliferation or survival of tumor cells that overexpress SHMT2 or inhibits maintenance, growth, or metastasis of a tumor that overexpresses SHMT2.

26. The method of claim 15, further comprising determining whether the test agent selectively inhibits proliferation or survival of tumor cells as compared with its effect on non-tumor cells.

27. The method of claim 15, further comprising determining whether the test agent selectively inhibits proliferation or survival of tumor cells that overexpress SHMT2, as compared with its effect on non-tumor cells.

28. The method of claim 15, further comprising administering the test agent to a subject suffering from a tumor.

29. The method of claim 15, further comprising producing an altered test agent and assessing the ability of the altered test agent to inhibit a GCS component, inhibit the GCS, inhibit the survival or proliferation of tumor cells, or inhibit the maintenance, growth, or metastasis of a tumor.

30. The method of claim 15, further comprising producing an altered test agent and assessing the ability of the altered test agent to inhibit a GCS component, inhibit the GCS, inhibit the survival or proliferation of tumor cells that overexpress SHMT2, or inhibit the maintenance, growth, or metastasis of a tumor that overexpresses SHMT2.

31. A method of identifying an anti-tumor agent, the method comprising (a) contacting a tumor cell, tumor cell line, or tumor with a GCS inhibitor; and (b) determining whether the survival, proliferation, growth, or metastasis of the tumor cell or tumor is inhibited, wherein if the survival, proliferation, growth, or metastasis of the tumor cell, tumor cell line, or tumor is inhibited, the GCS inhibitor is an anti-tumor agent.

32. The method of claim 31, wherein step (b) comprises comparing the survival, proliferation, growth, or metastasis of the tumor cell, tumor cell line, or tumor of (a) with a control value, wherein if survival, proliferation, growth, or metastasis of the tumor cell or tumor of (a) is reduced as compared with control value, the GCS inhibitor is identified as an anti-tumor agent.

33. The method of claim 31, wherein the tumor cell or tumor overexpresses SHMT2.

34. The method of claim 31, wherein the control value represents the survival, proliferation, growth, or metastasis of the tumor cell, tumor cell line, or tumor if not contacted with the GCS inhibitor.

35. A method of predicting the likelihood that a tumor, tumor cell, or tumor cell line is sensitive to GCS inhibition, the method comprising: (a) determining whether the tumor, tumor cell, or tumor cell line overexpresses SHMT2 or belongs to a tumor type that has a tendency to overexpress SHMT2, wherein if the tumor, tumor cell, or tumor cell line overexpresses SHMT2 or belongs to a tumor type that has a tendency to overexpress SHMT2, the tumor, tumor cell, or tumor cell line has increased likelihood of being sensitive to GCS inhibition than if tumor, tumor cell, or tumor cell line does not overexpress SHMT2 or does not belong to a tumor type that has a tendency to overexpress SHMT2.

36. The method of claim 35, wherein the method comprises determining whether tumor, tumor cell, or tumor cell line overexpresses SHMT2, wherein if the tumor, tumor cell, or tumor cell line overexpresses SHMT2 the tumor, tumor cell, or tumor cell line has increased likelihood of being sensitive to GCS inhibition than if the tumor, tumor cell, or tumor cell line does not overexpress SHMT2.

37. The method of claim 35, wherein determining whether a tumor or tumor cell line overexpresses SHMT2 comprises (a) determining the level of a SHMT2 gene product in a sample obtained from the tumor or tumor cell line; and (b) comparing the level with a control level of SHMT2 gene product, wherein if the level determined in (a) is greater than the control level, the tumor or tumor cell line has increased likelihood of being sensitive to GCS inhibition than if the level determined in (a) is not greater than the control level.

38. The method of claim 35, wherein the control level of SHMT2 gene product is a level of said gene product in non-tumor tissue or non-tumor cells.

39. The method of claim 35, wherein the SHMT2 gene product is a SHMT2 RNA or a SHMT2 polypeptide.

40. The method of claim 35, wherein determining whether a tumor overexpresses SHMT2 comprises performing immunohistochemistry (IHC) on a sample obtained from the tumor, using an antibody that binds to SHMT2 polypeptide.

41. The method of claim 35, wherein determining whether a tumor is of a tumor type that has a tendency to overexpress SHMT2 comprises determining whether the tumor is a brain tumor, bladder tumor, breast tumor, cervical tumor, colorectal tumor, embryonal tumor, gastric tumor, germ cell tumor, head and neck tumor, hematologic tumor, kidney tumor, melanoma, mesothelial tumor, ovarian tumor, yolk sac tumor, or sarcoma.

42. A method of identifying a tumor cell or tumor that has an increased likelihood of being sensitive to GCS inhibition, the method comprising assessing expression of SHMT2 in the tumor cell or tumor, wherein if the tumor cell or tumor overexpresses SHMT2, the tumor cell or tumor has an increased likelihood of being sensitive to GCS inhibition than if SHMT2 is not overexpressed.

43. The method of claim 42, wherein the method comprises assessing the level of an SHMT2 gene product in the tumor cell or tumor.

44. The method of claim 42, wherein the method comprises performing immunohistochemistry (IHC) on a sample obtained from the tumor, wherein IHC is performed using an antibody that binds to SHMT2 polypeptide.

45. A method of determining whether a subject in need of treatment for a tumor is a suitable candidate for treatment with a GCS inhibitor, the method comprising determining whether the tumor overexpresses SHMT2 or is of a tumor type that has a tendency to overexpress SHMT2, wherein if the tumor overexpresses SHMT2 or is of a tumor type that has a tendency to overexpress SHMT2, the subject is a suitable candidate for treatment with a GCS inhibitor.

46. The method of claim 45, wherein determining whether the tumor overexpresses SHMT2 comprises (a) determining the level of a SHMT2 gene product in a sample obtained from the tumor.

47. The method of claim 46, further comprising comparing the level with a control level of SHMT2 gene product, wherein if the level determined in (a) is greater than the control level, the subject is a suitable candidate for treatment with a GCS inhibitor.

48. The method of claim 47, wherein the control level of SHMT2 gene product is a level of said gene product in non-tumor tissue or non-tumor cells.

49. The method of claim 46, wherein the SHMT2 gene product is a SHMT2 RNA or a SHMT2 polypeptide.

50. The method of claim 46, wherein the method comprises performing immunohistochemistry (IHC) on a sample obtained from the tumor, wherein IHC is performed using an antibody that binds to SHMT2 polypeptide.

51. The method of claim 45, wherein determining whether the tumor is of a tumor type prone to overexpress SHMT2 comprises determining whether the tumor is a brain tumor, bladder tumor, breast tumor, cervical tumor, colorectal tumor, embryonal tumor, gastric tumor, germ cell tumor, head and neck tumor, hematologic tumor, kidney tumor, melanoma, mesothelial tumor, ovarian tumor, yolk sac tumor, or sarcoma.

52. An *in vitro* method of selecting a therapeutic agent for a subject in need of treatment for a tumor, the method comprising: (a) determining whether the tumor overexpresses SHMT2 or is of a tumor type that has a tendency to overexpress SHMT2; and (b) selecting a therapeutic agent for the subject based at least in part of the results of step (a).

53. The method of claim 52, wherein step (b) comprises selecting a GCS inhibitor as a therapeutic agent if the tumor overexpresses SHMT2 or is of a tumor type that has a tendency to overexpress SHMT2.

54. The method of claim 52, wherein step (a) comprises performing immunohistochemistry (IHC) on a sample obtained from the tumor, wherein IHC is performed using an antibody that binds to SHMT2 polypeptide.

55. Use of a GCS inhibitor in the manufacture of a medicament for treating a subject having a tumor.

56. The use of claim 55, wherein the tumor overexpresses SHMT2.

57. The use of claim 55, wherein the tumor is of a tumor type that has a tendency to overexpress SHMT2.

58. The use of claim 55, wherein the method comprises determining that the tumor overexpresses SHMT2.

59. The use of claim 55, wherein the method comprises determining that the tumor overexpresses SHMT2 by performing IHC on a sample obtained from the tumor.

60. The use of claim 55, wherein the method comprises determining that the tumor is sensitive to inhibition of the GCS.

61. The use of claim 55, wherein the method comprises determining that the subject is a suitable candidate for treatment with a GCS inhibitor to treat the tumor.

62. The use of claim 55, wherein the GCS inhibitor comprises an RNAi agent

63. The use of claim 55, wherein the GCS inhibitor comprises cysteamine or a cysteamine salt, analog, or prodrug.

64. The use of claim 55, wherein the GCS inhibitor is a GLDC inhibitor.

65. The use of claim 55, wherein the GCS inhibitor is a GCSH inhibitor.

66. The use of claim 55, wherein the tumor is a brain tumor, bladder tumor, breast tumor, cervical tumor, colorectal tumor, embryonal tumor, gastric tumor, germ cell tumor, head and neck tumor, hematologic tumor, kidney tumor, melanoma, mesothelial tumor, ovarian tumor, yolk sac tumor, or sarcoma.

67. The use of claim 55, wherein the tumor is a GBM.

68. The use of claim 55, further comprising administering radiation therapy to the subject.

69. The use of claim 55, further comprising administering a second anti-tumor agent to the subject.

70. Use of a GCS inhibitor in the manufacture of a medicament for treating a subject having a tumor that overexpresses SHMT2.

71. The use of claim 70, wherein determining that the tumor overexpresses SHMT2 comprises performing IHC on a sample obtained from the tumor.

72. The use of claim 70, wherein the GCS inhibitor comprises an RNAi agent.

73. The use of claim 70, wherein the GCS inhibitor comprises cysteamine or a cysteamine salt, prodrug, or analog.

74. The use of claim 70, wherein the GCS inhibitor is a GLDC inhibitor.

75. The use of claim 70, wherein the GCS inhibitor is a GCSH inhibitor.

76. The use of claim 70, wherein the tumor is a brain tumor, bladder tumor, breast tumor, cervical tumor, colorectal tumor, embryonal tumor, gastric tumor, germ cell tumor, head and neck tumor, hematologic tumor, kidney tumor, melanoma, mesothelial tumor, ovarian tumor, yolk sac tumor, or sarcoma.

77. The use of claim 70, wherein the tumor is a GBM.

78. The use of claim 70, further comprising treating the subject using radiation therapy.

79. The use of claim 70, further comprising treating the subject with a second anti-tumor agent.

80. A method of monitoring a subject in need of treatment for a tumor, the method comprisingmonitoring the subject at one or more time points after administration of a GCS inhibitor.

81. The method of claim 80, wherein the tumor overexpresses SHMT2.

82. The method of claim 80, wherein the GCS inhibitor comprises an RNAi agent

83. The method of claim 80, wherein the GCS inhibitor comprises cysteamine or a cysteamine salt, prodrug, or analog.

84. The method of claim 80, wherein the GCS inhibitor is a GLDC inhibitor.

85. The method of claim 80, wherein the GCS inhibitor is a GCSH inhibitor.

86. The method of claim 80, wherein the tumor is a brain tumor, bladder tumor, breast tumor, cervical tumor, colorectal tumor, embryonal tumor, gastric tumor, germ cell tumor, head and neck tumor, hematologic tumor, kidney tumor, melanoma, mesothelial tumor, ovarian tumor, yolk sac tumor, or sarcoma.

87. The method of claim 80, wherein the tumor is a GBM.

88. The method of claim 80, further comprising treating the subject using radiation therapy.

89. The method of claim 80, further comprising treating the subject with a second anti-tumor agent.

90. A pharmaceutical composition for anti-tumor therapy, comprising: (a) an effective amount of a GCS inhibitor; and (b) a pharmaceutically acceptable carrier.

91. A unit dosage form comprising a GCS inhibitor in an amount appropriate for administration to a subject for treatment of a tumor.

92. A composition comprising: (a) a GCS inhibitor; and (b) a second anti-tumor agent.

93. A kit comprising: (a) a reagent that binds to an SHMT2 gene product; and (b) at least one item selected from the group consisting of: (i) instructions for using the reagent to determine whether a tumor overexpresses SHMT2; (ii) a detection reagent; and (iii) a control reagent.

94. The kit of claim 93, wherein the reagent of (a) comprises an antibody that binds to SHMT2 polypeptide.

95. The kit of claim 93, wherein the reagent of (a) comprises a probe or primer that binds to mRNA encoding SHMT2 polypeptide.