

of at least one gene set forth in Table 1 in a sample obtained from the patient, wherein an increased expression level of the at least one gene in the sample as compared to a reference sample indicates that the patient may benefit from treatment with the anti-cancer therapy other than or in addition to a VEGF antagonist.

[0008a] Disclosed is a method of identifying a patient who may benefit from treatment with an anti-cancer therapy other than or in addition to a VEGF-A antagonist, the method comprising: determining expression levels of at least one gene set forth in Table 1 in a sample obtained from the patient, wherein an increased expression level of said at least one gene in the sample as compared to a reference sample indicates that the patient may benefit from treatment with the anti-cancer therapy.

[0009] Another embodiment of the invention provides methods of identifying a patient who may benefit from treatment with an anti-cancer therapy other than or in addition to a VEGF antagonist. The methods comprise: determining expression levels of at least one gene set forth in Table 1 in a sample obtained from the patient, wherein a decreased expression level of the at least one gene in the sample as compared to a reference sample indicates that the patient may benefit from treatment with the anti-cancer therapy other than or in addition to a VEGF antagonist.

[0009a] In one aspect, there is provided a method of identifying a patient who may benefit from treatment with an anti-cancer therapy comprising a VEGF-A antagonist, the method comprising: determining the expression level of VEGF-A in a sample obtained from the patient, wherein a decrease in the expression level of VEGF-A as compared to a reference sample identifies the patient as one who may benefit from treatment with the anti-cancer therapy.

[0009b] Disclosed is a method of optimizing therapeutic efficacy for treatment of cancer, the method comprising determining expression levels of at least one gene set forth in Table 1 in a sample obtained from the patient, wherein an increased expression level of said at least one gene in the sample as compared to a reference sample indicates that the patient has increased likelihood of benefit from an anti-cancer therapy other than or in addition to a VEGF-A antagonist.

[0009c] In one aspect, there is provided a method of optimizing therapeutic efficacy for treatment of cancer, the method comprising: determining the expression level of VEGF-A in a sample obtained from the patient, wherein a decrease in the expression level of VEGF-A as compared to a reference sample indicates that the patient may benefit from an anti-cancer therapy comprising a VEGF-A antagonist.

has increased likelihood of benefit from the anti-cancer therapy other than or in addition to a VEGF antagonist.

[0013] Another embodiment of the invention provides methods for determining the likelihood that a patient with cancer will exhibit benefit from anti-cancer therapy other than or in addition to a VEGF antagonist. The methods comprise: determining expression levels of at least one gene set forth in Table 1 in a sample obtained from the patient, wherein a decreased expression level of the at least one gene in the sample as compared to a reference sample indicates that the patient has increased likelihood of benefit from the anti-cancer therapy other than or in addition to a VEGF antagonist.

[0014] A further embodiment of the invention provides methods for treating cancer in a patient. The methods comprise: determining that a sample obtained from the patient has increased expression levels, as compared to a reference sample, of at least one gene set forth in Table 1, and administering an effective amount of an anti-cancer therapy other than or in addition to a VEGF antagonist to the patient, whereby the cancer is treated.

[0015] Another embodiment of the invention provides methods for treating cancer in a patient. The methods comprise determining that a sample obtained from the patient has decreased expression levels, as compared to a reference sample, of at least one gene set forth in Table 1, and administering an effective amount of an anti-cancer therapy other than or in addition to a VEGF antagonist to the patient, whereby the cancer is treated.

[0015a] In one aspect, there is provided use of a VEGF-A antagonist in the manufacture of a medicament for treating cancer in a patient, wherein treating comprises determining the expression level of VEGF-A in a sample obtained from the patient, wherein a decrease in the expression level of VEGF-A as compared to a reference sample identifies the patient as one who may benefit from treatment with the medicament.

[0016] In some embodiments of the invention, the sample obtained from the patient is selected from: tissue, whole blood, blood-derived cells, plasma, serum, and combinations thereof. In some embodiments of the invention, the expression level is mRNA expression level. In some embodiments of the invention, the expression level is protein expression level.

[0017] In some embodiments of the invention, the methods further comprise detecting the expression of at least a second, third, fourth, fifth, sixth, seventh, eighth, ninth, tenth, eleventh, twelfth, thirteenth, fourteenth, fifteenth, sixteenth, seventeenth, eighteenth, nineteenth, or twentieth gene set forth in Table 1.

[0018] In some embodiments of the invention, the methods further comprising administering the anti-cancer therapy other than a VEGF antagonist to the patient. In some embodiments of the invention, the anti-cancer therapy is selected from: an

level of the at least one gene in a reference sample indicates that the patient may benefit from treatment with a VEGF-C antagonist. In some embodiments of the invention, the compounds are polynucleotides. In some embodiments of the invention, the compounds are proteins, such as, for example, antibodies.

[0103] One embodiment of the invention provides methods of identifying a patient suffering from cancer who may benefit from treatment with an EGF-like-domain, multiple 7 (EGFL7) antagonist. The methods comprise determining expression levels of at least one gene selected from: VEGF-C, BV8, CSF2, TNF α , CXCL2, PDGF-C, and Mincle in a sample obtained from the patient, wherein increased expression levels of the at least one gene in the sample as compared to a reference sample indicates that the patient may benefit from treatment with the EGFL7 antagonist.

[0103a] Disclosed is a method of identifying a patient suffering from cancer who may benefit from treatment with an EGF-like-domain, multiple 7 (EGFL7) antagonist, the method comprising determining expression levels of at least one gene selected from the group consisting of: VEGF-C, BV8, CSF2, TNF α , CXCL2, PDGF-C, and Mincle in a sample obtained from the patient, wherein increased expression levels of said at least one gene in the sample as compared to a reference sample indicates that the patient may benefit from treatment with the EGFL7 antagonist.

[0104] Another embodiment of the invention provides methods of identifying a patient suffering from cancer who may benefit from treatment with an EGFL7 antagonist. The methods comprise determining expression levels of at least one gene selected from: Sema3B, FGF9, HGF, RGS5, NRP1, FGF2, CXCR4, cMet, FN1, Fibulin 2, Fibulin4/EFEMP2, MFAP5, PDGF-C, Sema3F, and FN1 in a sample obtained from the patient, wherein decreased expression levels of the at least one gene in the sample as compared to a reference sample indicates that the patient may benefit from treatment with the EGFL7 antagonist.

[0104a] Disclosed is a method of identifying a patient suffering from cancer who may benefit from treatment with an EGFL7 antagonist, the method comprising determining expression levels of at least one gene selected from the group consisting of: Sema3B, FGF9, HGF, RGS5, NRP1, FGF2, CXCR4, cMet, FN1, Fibulin 2, Fibulin4/EFEMP2, MFAP5, PDGF-C, Sema3F, and FN1 in a sample obtained from the patient, wherein decreased expression levels of said at least one gene in the sample as compared to a reference sample indicates that the patient may benefit from treatment with the EGFL7 antagonist

[0105] A further embodiment of the invention provides methods of predicting responsiveness of a patient suffering from cancer to treatment with an EGFL7 antagonist. The methods comprise determining expression levels of at least one gene selected from: VEGF-C, BV8, CSF2, TNF α , CXCL2, PDGF-C, and Mincle in a sample obtained from the patient, wherein increased expression levels of the at least one gene in the sample as compared to a reference sample indicates that the patient is more likely to be responsive to treatment with the EGFL7 antagonist.

[0106] Yet another embodiment of the invention provides methods of predicting responsiveness of a patient suffering from cancer to treatment with an EGFL7 antagonist. The methods comprise determining expression levels of at least one gene selected from: Sema3B, FGF9, HGF, RGS5, NRP1, FGF2, CXCR4, cMet, FN1, Fibulin 2, Fibulin4/EFEMP2, MFAP5, PDGF-C, Sema3F, and FN1 in a sample obtained from the patient, wherein decreased expression levels of the at least one gene

in the sample as compared to a reference sample indicates that the patient is more likely to be responsive to treatment with the EGFL7 antagonist.

[0107] Even another embodiment of the invention provides methods of determining the likelihood that a patient will exhibit a benefit from treatment with an EGFL7 antagonist. The methods comprise determining expression levels of at least one gene selected from: VEGF-C, BV8, CSF2, TNF α , CXCL2, PDGF-C, and Mincle in a sample obtained from the patient, wherein increased expression levels of the at least one gene in the sample as compared to a reference sample indicates that the patient has increased likelihood of benefit from treatment with the EGFL7 antagonist.

[0108] Yet a further embodiment of the invention provides methods of determining the likelihood that a patient will exhibit a benefit from treatment with an EGFL7 antagonist. The methods comprise determining expression levels of at least one gene selected from: Sema3B, FGF9, HGF, RGS5, NRP1, FGF2, CXCR4, cMet, FN1, Fibulin 2, Fibulin4/EFEMP2, MFAP5, PDGF-C, Sema3F, and FN1 in a sample obtained from the patient, wherein decreased expression levels of the at least one gene in the sample as compared to a reference sample indicates that the patient has increased likelihood of benefit of treatment with the EGFL7 antagonist.

[0109] Even another embodiment of the invention provides methods of optimizing therapeutic efficacy of an EGFL7 antagonist. The methods comprise determining expression levels of at least one gene selected from: VEGF-C, BV8, CSF2, TNF α , CXCL2, PDGF-C, and Mincle in a sample obtained from the patient, wherein increased expression levels of the at least one gene in the sample as compared to a reference sample indicates that the patient has increased likelihood of benefit from treatment with the EGFL7 antagonist.

[0109a] Disclosed is a method of optimizing therapeutic efficacy of an EGFL7 antagonist, the method comprising determining expression levels of at least one gene selected from the group consisting of: VEGF-C, BV8, CSF2, TNF α , CXCL2, PDGF-C, and Mincle in a sample obtained from a patient, wherein increased expression levels of said at least one gene in the sample as compared to a reference sample indicates that the patient has increased likelihood of benefit from treatment with the EGFL7 antagonist.

[0110] Yet a further embodiment of the invention provides methods of optimizing therapeutic efficacy of an EGFL7 antagonist. The methods comprise determining expression levels of at least one gene selected from: Sema3B, FGF9, HGF, RGS5, NRP1, FGF2, CXCR4, cMet, FN1, Fibulin 2, Fibulin4/EFEMP2, MFAP5, PDGF-C, Sema3F, and FN1 in a sample obtained from the patient, wherein decreased expression levels of the at least one gene in the sample as compared to a reference sample indicates that the patient has increased likelihood of benefit of treatment with the EGFL7 antagonist.

[0110a] Disclosed is a method of optimizing therapeutic efficacy of an EGFL7 antagonist, the method comprising determining expression levels of at least one gene selected from the group consisting of: Sema3B, FGF9, HGF, RGS5, NRP1, FGF2, CXCR4, cMet, FN1, Fibulin 2, Fibulin4/EFEMP2, MFAP5, PDGF-C, Sema3F, and FN1 in a sample obtained from a patient, wherein decreased expression levels of said at least one gene in the sample as compared to a reference sample indicates that the patient has increased likelihood of benefit of treatment with the EGFL7 antagonist.

[0111] Another embodiment of the invention provides methods for treating a cell proliferative disorder in a patient. The methods comprise determining

that a sample obtained from the patient has increased expression levels, as compared to a reference sample, of at least one gene selected from: VEGF-C, BV8, CSF2, TNF α , CXCL2, PDGF-C, and Mincle, and administering to the patient an effective amount of an EGFL7 antagonist, whereby the cell proliferative disorder is treated.

[0111a] Disclosed is use of an EGFL7 antagonist in the manufacture of a medicament for the treatment of a cell proliferative disorder in a patient, wherein the patient is one whose sample has increased expression levels, as compared to a reference sample, of at least one gene selected from the group consisting of: VEGF-C, BV8, CSF2, TNF α , CXCL2, PDGF-C, and Mincle.

[0112] A further embodiment of the invention provides methods for treating a cell proliferative disorder in a patient. The methods comprise determining that a sample obtained from the patient has decreased expression levels, as compared to a reference sample, of at least one gene selected from: Sema3B, FGF9, HGF, RGS5, NRP1, FGF2, CXCR4, cMet, FN1, Fibulin 2, Fibulin4/EFEMP2, MFAP5, PDGF-C, Sema3F, and FN1, and administering to the patient an effective amount of an EGFL7 antagonist, whereby the cell proliferative disorder is treated.

[0112a] Disclosed is use of an EGFL7 antagonist in the manufacture of a medicament for the treatment of a cell proliferative disorder in a patient, wherein the patient is one whose sample has decreased expression levels, as compared to a reference sample, of at least one gene selected from the group consisting of: Sema3B, FGF9, HGF, RGS5, NRP1, FGF2, CXCR4, cMet, FN1, Fibulin 2, Fibulin4/EFEMP2, MFAP5, PDGF-C, Sema3F, and FN1.

[0113] In some embodiments of the invention, the sample obtained from the patient is selected from: tissue, whole blood, blood-derived cells, plasma, serum, and combinations thereof. In some embodiments of the invention, the expression level is mRNA expression level. In some embodiments of the invention, the expression level is protein expression level. In some embodiments of the invention, the EGFL7 antagonist is an anti-EGFL7 antibody.

[0114] In some embodiments of the invention, the methods further comprises administering a VEGF-A antagonist to the patient. In some embodiments of the invention, the VEGF-A antagonist and the EGFL7 antagonist are administered concurrently. In some embodiments of the invention, the VEGF-A antagonist and the EGFL7 antagonist are administered sequentially. In some embodiments of the invention, the VEGF-A antagonist is an anti-VEGF-A antibody. In some embodiments of the invention, the anti-VEGF-A antibody is bevacizumab.

[0115] A further embodiment of the invention provides methods of identifying a patient suffering from cancer who may benefit from treatment with an EGFL7 antagonist. The methods comprise determining expression levels of VEGF-C in a sample obtained from the patient, wherein increased expression levels of VEGF-C in the sample as compared to a reference sample indicates that the patient may benefit from treatment with the EGFL7 antagonist.

[0116] Another embodiment of the invention provides methods of predicting responsiveness of a patient suffering from cancer to treatment with an EGFL7 antagonist. The methods comprise determining expression levels of VEGF-C in a sample obtained from the patient, wherein increased expression levels of VEGF-

CLAIMS

1. A method of identifying a patient who may benefit from treatment with an anti-cancer therapy comprising a VEGF-A antagonist, the method comprising:

determining the expression level of VEGF-A in a sample obtained from the patient, wherein a decrease in the expression level of VEGF-A as compared to a reference sample identifies the patient as one who may benefit from treatment with the anti-cancer therapy.

2. A method of optimizing therapeutic efficacy for treatment of cancer, the method comprising:

determining the expression level of VEGF-A in a sample obtained from the patient, wherein a decrease in the expression level of VEGF-A as compared to a reference sample indicates that the patient may benefit from an anti-cancer therapy comprising a VEGF-A antagonist.

3. The method of claim 1 or 2, further comprising determining the expression level of at least one other gene set forth in Table 1 in a sample obtained from the patient, wherein a change in the expression level of said at least one other gene in the sample as compared to a reference sample indicates that the patient may benefit from treatment with the anti-cancer therapy.

4. The method of claim 3, wherein the change is an increase.

5. The method of claim 3, wherein the change is a decrease.

6. The method of any one of claims 1-5, wherein the sample obtained from the patient is a member selected from the group consisting of: tissue, whole blood, blood-derived cells, plasma, serum, and a combination thereof.

7. The method of any one of claims 1-6, wherein the expression level is selected from mRNA expression level, protein expression level, and a combination thereof.

8. The method of any one of claims 1-7, further comprising detecting the expression of at least a second, third, fourth, fifth, sixth, seventh, eighth, ninth, or tenth other gene set forth in Table 1.

9. The method of any one of claims 1-8, wherein the VEGF-A antagonist is an anti-VEGF-A antibody.

10. The method of claim 9, wherein the anti-VEGF-A antibody is bevacizumab.

11. Use of a VEGF-A antagonist in the manufacture of a medicament for treating cancer in a patient, wherein treating comprises determining the expression level of VEGF-A in a sample obtained from the patient, wherein a decrease in the expression level of VEGF-A as compared to a reference sample identifies the patient as one who may benefit from treatment with the medicament.

12. The use of claim 11, wherein the VEGF-A antagonist is an anti-VEGF-A antibody.

13. The use of claim 12, wherein the anti-VEGF-A antibody is bevacizumab.

14. The use of any one of claims 11-13, wherein the VEGF-A antagonist is formulated for administration with an anti-cancer therapy other than a VEGF-A antagonist.

15. The use of claim 14, wherein the anti-cancer therapy other than a VEGF-A antagonist is a member selected from the group consisting of: an antibody, a small molecule, and an siRNA.

16. The use of claim 15, wherein the anti-cancer therapy other than a VEGF-A antagonist is a member selected from the group consisting of: an EGFL7 antagonist, a NRP1 antagonist, and a VEGF-C antagonist.

17. The use of claim 16, wherein the EGFL7 antagonist is an antibody.

18. The use of claim 16, wherein the NRP1 antagonist is an antibody.

19. The use of claim 16, wherein the VEGF-C antagonist is an antibody.

20. The use of any one of claims 14-19, wherein the anti-cancer therapy other than a VEGF-A antagonist and the VEGF-A antagonist are formulated for concurrent administration.

21. The use of any one of claims 14-19, wherein the anti-cancer therapy other than a VEGF-A antagonist and the VEGF-A antagonist are formulated for sequential administration.