BRIEF SUMMARY ~~OF THE INVENTION~~

[0006] ~~In a first aspect, the present invention provides~~Provided herein is a compound comprising a CLPTM1L-targeting agent selected from the group consisting of an antibody, a peptide, an aptamer, or a fragment thereof. In one aspect, provided herein is a CLPTM1L-targeting agent selected from the group consisting of an antibody, a peptide, and a peptide aptamer, or a fragment thereof. The CLPTM1L-targeting agent can be a monoclonal antibody specific for at least a portion of a CLPTM1L polypeptide. The CLPTM1L polypeptide can have the amino acid sequence set forth in SEQ ID NO: 2 or a portion thereof. The monoclonal antibody can be specific to peptide having an amino acid sequence selected from the group consisting of SEQ ID NO:4-25. The monoclonal antibody can be a monoclonal anti-CLPTM1L clone selected from the group consisting of 6-1, 6-2, 10-1, 10-2, and 10-3. The monoclonal antibody can be specific to a CLPTM1L polypeptide having one or more of the mutations set forth in Table 2. In some cases, the CLPTM1L-targeting agent is a peptide having an amino acid sequence selected from the group consisting of SEQ ID NO:4-25.

[0007] In another aspect, ~~the present invention provides~~provided herein is a pharmaceutical composition comprising a compound provided herein and a pharmaceutically acceptable carrier.

[0008] ~~In yet another aspect, p~~Provided herein is an agent according to a compound or composition provided herein for use as a medicament. In one aspect, provided herein is an agent as described above for use as a medicament. ~~Further~~ In another aspect, provided is use of such an agent in the manufacture of a medicament.

[0009] ~~In a further aspect, p~~Provided herein is an article of manufacture comprising a pharmaceutical composition of the ~~invention~~ disclosure and instructions for administration to a human subject. In one aspect, provided herein is an article of manufacture comprising: (a) the pharmaceutical composition as described above, and (b) an insert providing instructions for treating a solid tumor in a human subject.

[0010] In one aspect, provided herein is use of a compound comprising a CLPTM1L-targeting agent in the manufacture of a medicament for treating or preventing a tumor in a subject in need thereof, whereby the tumor is treated or prevented in the subject. ~~In another aspect,~~ Also provided herein is a method for treating or preventing a tumor pre- in a subject. The use or method typically comprises administering a therapeutically effective amount of a compound comprising a CLPTM1L-targeting agent to a subject in need thereof, whereby the tumor is treated or prevented in the subject. In some cases, the CLPTM1L-targeting agent is selected from the group consisting of an antibody, a peptide, and aptamer, or a fragment thereof. The CLPTM1L-targeting agent can be a monoclonal antibody specific for at least a portion of a CLPTM1L polypeptide. The CLPTM1L polypeptide can have the amino acid sequence set forth in SEQ ID NO:2 or a portion thereof. The monoclonal antibody can be specific to a peptide having an amino acid sequence selected from the group consisting of SEQ ID NO:4-25. The monoclonal antibody can be specific to a CLPTM1L polypeptide having one or more of the mutations set forth in Table 2. The CLPTM1L-targeting agent can be a peptide having an amino acid sequence selected from the group consisting of SEQ ID NO:4-25.

[0011] In some cases, the tumor is a solid tumor selected from the group consisting of glioblastoma, sarcoma, carcinoma, and lymphoma. In some cases, the tumor is associated with

a cancer or pre-neoplastic lesion selected from the group consisting of lung cancer, pancreatic cancer, prostate cancer, skin cancer, bladder cancer, kidney cancer, ovarian cancer, colon cancer, colorectal cancer, breast cancer, cervical cancer, brain cancer, esophageal cancer, and stomach cancer, or a pre-neoplastic lesion thereof. The tumor can be associated with lung cancer or a pre-neoplastic lesion thereof. The tumor can exhibit resistance to a chemotherapeutic agent. The chemotherapeutic agent can be selected from the group consisting of cisplatin and gemcitabine. In some cases, the compound is administered with a pharmaceutically acceptable carrier.

[0012] In yet another aspect, provided herein is use of a compound comprising a CLPTM1L-targeting agent in the manufacture of a medicament for treating or preventing a disease or condition associated with CLPTM1L protein dysfunction, wherein the medicament is to be administered to a cell, tissue, or organ of a subject at risk of, diagnosed as having, or exhibiting a symptom of the disease or condition. Also provided herein is a method of treating or preventing a disease or condition associated with over-expression or inappropriate expression of a nucleic acid sequence encoding CLPTM1L in a subject. The use or method typically comprises administering a compound comprising a CLPTM1L-targeting agent to a cell, tissue, or organ of a subject at risk of, diagnosed as having, or exhibiting a symptom of the disease or condition. The disease or condition can be a cancer, tumor, (*e.g.*, solid tumor) or a pre-neoplastic lesion. The tumor, cancer, or pre-neoplastic lesion can be selected from the group consisting of lung cancer, pancreatic cancer, glioblastoma, prostate cancer, skin cancer, bladder cancer, kidney cancer, ovarian cancer, colon cancer, colorectal cancer, breast cancer, cervical cancer, brain cancer, esophageal cancer, stomach cancer, lymphoma, chronic leukemia, and acute leukemia. The tumor can exhibit resistance to a chemotherapeutic agent. The chemotherapeutic agent can be selected from the group consisting of cisplatin and gemcitabine. The CLPTM1L-targeting agent can be selected from the group consisting of an antibody, a peptide, and aptamer, or a fragment thereof. The CLPTM1L-targeting agent can be a monoclonal antibody specific for at least a portion of a CLPTM1L polypeptide. The CLPTM1L polypeptide can have the amino acid sequence set forth in SEQ ID NO: 2 or a portion thereof. In some cases, the monoclonal antibody is specific to a peptide having an amino acid sequence selected from the group consisting of SEQ ID NO:4-25. The monoclonal antibody can be specific to a CLPTM1L polypeptide having one or more of the mutations set forth in Table 2. The CLPTM1L-targeting agent can be a peptide having an amino acid sequence selected from the group consisting of SEQ ID NO:4-25. The compound can be administered with a pharmaceutically acceptable carrier.

[0013] These and other features, aspects, and advantages of the present invention will become better understood from the description that follows. In the description, reference is made to the accompanying drawings, which form a part hereof and in which there is shown by way of illustration, not limitation, embodiments of the ~~invention~~disclosure. The description of preferred

CLAIMS

We claim:

1. A CLPTM1L-targeting agent selected from the group consisting of an antibody, a peptide, and an aptamer, or a fragment thereof.

2. The agent of claim 1, wherein the CLPTM1L-targeting agent is a monoclonal antibody specific for at least a portion of a CLPTM1L polypeptide.

3. The agent of claim 2, wherein the CLPTM1L polypeptide has the amino acid sequence set forth in SEQ ID NO:2 or a portion thereof.

4. The agent of claim 2, wherein the monoclonal antibody is specific to peptide having an amino acid sequence selected from the group consisting of SEQ ID NO:4-25.

5. The agent of claim 2, wherein the monoclonal antibody is a monoclonal anti-CLPTM1L clone selected from the group consisting of 6-1, 6-2, 10-1, 10-2, and 10-3.

6. The agent of claim 2, wherein the monoclonal antibody is specific to a CLPTM1L polypeptide having one or more of the mutations set forth in Table 2.

7. The agent of claim 1, wherein the CLPTM1L-targeting agent is a peptide having an amino acid sequence selected from the group consisting of SEQ ID NO:4-25.

8. A pharmaceutical composition comprising the compound according to any of claims 1-6 and a pharmaceutically acceptable carrier.

9. The agent according to any of claims 1-7 for use as a medicament.

10. Use of the agent according to any of claims 1-7 in the manufacture of a medicament.

11. An article of manufacture comprising: (a) the pharmaceutical composition of claim 8, and (b) an insert providing instructions for treating a solid tumor in a human subject.

12. A method for treating or preventing a tumor comprising administering to a subject in need thereof a therapeutically effective amount of a compound comprising a CLPTM1L-targeting agent to a subject in need thereof, whereby the tumor is treated or prevented in the subject.

13. The method of claim 12, wherein the CLPTM1L-targeting agent is selected from the group consisting of an antibody, a peptide, and aptamer, or a fragment thereof.

14. The method of claim 12, wherein the CLPTM1L-targeting agent is a monoclonal antibody specific for at least a portion of a CLPTM1L polypeptide.

15. The method of claim 14, wherein the CLPTM1L polypeptide has the amino acid sequence set forth in SEQ ID NO:2 or a portion thereof.

16. The method of claim 14, wherein the monoclonal antibody is specific to a peptide having an amino acid sequence selected from the group consisting of SEQ ID NO:4-25.

17. The method of claim 12, wherein the CLPTM1L targeting moiety is a peptide having an amino acid sequence selected from the group consisting of SEQ ID NO:4-25.

18. The method of claim 12, wherein the tumor is a solid tumor selected from the group consisting of glioblastoma, sarcoma, carcinoma, and lymphoma.

19. The method of claim 12, wherein the tumor is associated with a cancer or pre-neoplastic lesion selected from the group consisting of lung cancer, pancreatic cancer, prostate cancer, skin cancer, bladder cancer, kidney cancer, ovarian cancer, colon cancer, colorectal cancer, breast cancer, cervical cancer, brain cancer, esophageal cancer, and stomach cancer, or a pre-cancerous lesion thereof.

20. The method of claim 19, wherein the tumor is associated with lung cancer or pre-cancerous lesion thereof.

21. The method of claim 12, wherein the subject is a human.

22. The method of claim 12, wherein the tumor exhibits resistance to a chemotherapeutic agent.

23. The method of claim 22, wherein the chemotherapeutic agent is selected from the group consisting of cisplatin and gemcitabine.

24. The method of claim 12, wherein the compound is administered with a pharmaceutically acceptable carrier.

25. A method of treating or preventing a disease or condition associated with CLPTM1L protein dysfunction, the method comprising administering a compound comprising a CLPTM1L-targeting agent to a cell, tissue, or organ of a subject at risk of, diagnosed as having, or exhibiting a symptom of the disease or condition.

26. The method of claim 25, wherein the CLPTM1L protein dysfunction comprises one or more of pathogenic protein production, pathogenic protein modification, or pathogenic protein function.

27. The method of claim 25, wherein the disease or condition is a tumor, a cancer, or a pre-neoplastic lesion.

28. The method of claim 27, wherein the tumor is a solid tumor selected from the group consisting of glioblastoma, sarcoma, carcinoma, and lymphoma.

29. The method of claim 28, wherein the tumor exhibits resistance to a chemotherapeutic agent.

30. The method of claim 29, wherein the chemotherapeutic agent is selected from the group consisting of cisplatin and gemcitabine

31. The method of claim 25, wherein the CLPTM1L-targeting agent is selected from the group consisting of an antibody, a peptide, and aptamer, or a fragment thereof.

32. The method of claim 25, wherein the CLPTM1L-targeting agent is a monoclonal antibody specific for at least a portion of a CLPTM1L polypeptide.

33. The method of claim 32, wherein the monoclonal antibody is specific to a CLPTM1L polypeptide having one or more of the mutations set forth in Table 2.

34. The method of claim 32, wherein the monoclonal antibody is specific to a peptide having an amino acid sequence selected from the group consisting of SEQ ID NO:4-25.

35. The method of claim 25, wherein the compound is administered with a pharmaceutically acceptable carrier.

AMENDED CLAIMS
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CLAIMS

We claim:

1. A CLPTM1L-targeting agent selected from the group consisting of an antibody, a peptide, and a peptide aptamer, or a fragment thereof.

2. The agent of claim 1, wherein the CLPTM1L-targeting agent is a monoclonal antibody specific for at least a portion of a CLPTM1L polypeptide.

3. The agent of claim 2, wherein the CLPTM1L polypeptide has the amino acid sequence set forth in SEQ ID NO:2 or a portion thereof.

4. The agent of claim 2, wherein the monoclonal antibody is specific to peptide having an amino acid sequence selected from the group consisting of SEQ ID NO:4-25.

5. The agent of claim 2, wherein the monoclonal antibody is a monoclonal anti-CLPTM1L clone selected from the group consisting of 6-1, 6-2, 10-1, 10-2, and 10-3.

6. The agent of claim 2, wherein the monoclonal antibody is specific to a CLPTM1L polypeptide having one or more of the mutations set forth in Table 2.

7. The agent of claim 1, wherein the CLPTM1L-targeting agent has specificity for an epitope having an amino acid sequence selected from the group consisting of SEQ ID NO:4-25.

8. A pharmaceutical composition comprising the compound according to any of claims 1-6 and a pharmaceutically acceptable carrier.

9. The agent according to any of claims 1-7 for use as a medicament.

10. Use of the agent according to any of claims 1-7 in the manufacture of a medicament.

11. An article of manufacture comprising: (a) the pharmaceutical composition of claim 8, and (b) an insert providing instructions for treating a solid tumor in a human subject.

12. A method for treating or preventing a tumor comprising administering to a subject in need thereof a therapeutically effective amount of a compound comprising a CLPTM1L-targeting agent to a subject in need thereof, whereby the tumor is treated or prevented in the subject.

13. The method of claim 12, wherein the CLPTM1L-targeting agent is selected from the group consisting of an antibody, a peptide, and aptamer, or a fragment thereof.

14. The method of claim 12, wherein the CLPTM1L-targeting agent is a monoclonal antibody specific for at least a portion of a CLPTM1L polypeptide.

15. The method of claim 14, wherein the CLPTM1L polypeptide has the amino acid sequence set forth in SEQ ID NO:2 or a portion thereof.

16. The method of claim 14, wherein the monoclonal antibody is specific to a peptide having an amino acid sequence selected from the group consisting of SEQ ID NO:4-25.

17. The method of claim 12, wherein the CLPTM1L targeting moiety has specificity for an epitope having an amino acid sequence selected from the group consisting of SEQ ID NO:4-25.

18. The method of claim 12, wherein the tumor is a solid tumor selected from the group consisting of glioblastoma, sarcoma, carcinoma, and lymphoma.

19. The method of claim 12, wherein the tumor is associated with a cancer or pre-neoplastic lesion selected from the group consisting of lung cancer, pancreatic cancer, prostate cancer, skin cancer, bladder cancer, kidney cancer, ovarian cancer, colon cancer, colorectal cancer, breast cancer, cervical cancer, brain cancer, esophageal cancer, and stomach cancer, or a pre-cancerous lesion thereof.

20. The method of claim 19, wherein the tumor is associated with lung cancer or pre-cancerous lesion thereof.

21. The method of claim 12, wherein the subject is a human.

22. The method of claim 12, wherein the tumor exhibits resistance to a chemotherapeutic agent.

23. The method of claim 22, wherein the chemotherapeutic agent is selected from the group consisting of cisplatin and gemcitabine.

24. The method of claim 12, wherein the compound is administered with a pharmaceutically acceptable carrier.

25. A method of treating or preventing a disease or condition associated with CLPTM1L protein dysfunction, the method comprising administering a compound comprising a CLPTM1L-targeting agent to a cell, tissue, or organ of a subject at risk of, diagnosed as having, or exhibiting a symptom of the disease or condition.

26. The method of claim 25, wherein the CLPTM1L protein dysfunction comprises one or more of pathogenic protein production, pathogenic protein modification, or pathogenic protein function.

27. The method of claim 25, wherein the disease or condition is a tumor, a cancer, or a pre-neoplastic lesion.

28. The method of claim 27, wherein the tumor is a solid tumor selected from the group consisting of glioblastoma, sarcoma, carcinoma, and lymphoma.

29. The method of claim 28, wherein the tumor exhibits resistance to a chemotherapeutic agent.

30. The method of claim 29, wherein the chemotherapeutic agent is selected from the group consisting of cisplatin and gemcitabine

31. The method of claim 25, wherein the CLPTM1L-targeting agent is selected from the group consisting of an antibody, a peptide, and aptamer, or a fragment thereof.

32. The method of claim 25, wherein the CLPTM1L-targeting agent is a monoclonal antibody specific for at least a portion of a CLPTM1L polypeptide.

33. The method of claim 32, wherein the monoclonal antibody is specific to a CLPTM1L polypeptide having one or more of the mutations set forth in Table 2.

34. The method of claim 32, wherein the monoclonal antibody is specific to a peptide having an amino acid sequence selected from the group consisting of SEQ ID NO:4-25.

35. The method of claim 25, wherein the compound is administered with a pharmaceutically acceptable carrier.

CLAIMS

We claim:

1. A CLPTM1L-targeting agent selected from the group consisting of an antibody, a peptide, and a peptide aptamer, or a fragment thereof.

2. The agent of claim 1, wherein the CLPTM1L-targeting agent is a monoclonal antibody specific for at least a portion of a CLPTM1L polypeptide.

3. The agent of claim 2, wherein the CLPTM1L polypeptide has the amino acid sequence set forth in SEQ ID NO:2 or a portion thereof.

4. The agent of claim 2, wherein the monoclonal antibody is specific to peptide having an amino acid sequence selected from the group consisting of SEQ ID NO:4-25.

5. The agent of claim 2, wherein the monoclonal antibody is a monoclonal anti-CLPTM1L clone selected from the group consisting of 6-1, 6-2, 10-1, 10-2, and 10-3.

6. The agent of claim 2, wherein the monoclonal antibody is specific to a CLPTM1L polypeptide having one or more of the mutations set forth in Table 2.

7. The agent of claim 1, wherein the CLPTM1L-targeting agent has specificity for an epitope having an amino acid sequence selected from the group consisting of SEQ ID NO:4-25.

8. A pharmaceutical composition comprising the compound according to any of claims 1-6 and a pharmaceutically acceptable carrier.

9. The agent according to any of claims 1-7 for use as a medicament.

10. Use of the agent according to any of claims 1-7 in the manufacture of a medicament.

11. An article of manufacture comprising: (a) the pharmaceutical composition of claim 8, and (b) an insert providing instructions for treating a solid tumor in a human subject.

12. Use of a compound comprising a CLPTM1L-targeting agent in the manufacture of a medicament for treating or preventing a tumor in a subject in need thereof, whereby the tumor is treated or prevented in the subject.

13. The use of claim 12, wherein the CLPTM1L-targeting agent is selected from the group consisting of an antibody, a peptide, and aptamer, or a fragment thereof.

14. The use of claim 12, wherein the CLPTM1L-targeting agent is a monoclonal antibody specific for at least a portion of a CLPTM1L polypeptide.

15. The use of claim 14, wherein the CLPTM1L polypeptide has the amino acid sequence set forth in SEQ ID NO:2 or a portion thereof.

16. The use of claim 14, wherein the monoclonal antibody is specific to a peptide having an amino acid sequence selected from the group consisting of SEQ ID NO:4-25.

17. The use of claim 12, wherein the CLPTM1L targeting moiety has specificity for an epitope having an amino acid sequence selected from the group consisting of SEQ ID NO:4-25.

18. The use of claim 12, wherein the tumor is a solid tumor selected from the group consisting of glioblastoma, sarcoma, carcinoma, and lymphoma.

19. The use of claim 12, wherein the tumor is associated with a cancer or pre-neoplastic lesion selected from the group consisting of lung cancer, pancreatic cancer, prostate cancer, skin cancer, bladder cancer, kidney cancer, ovarian cancer, colon cancer, colorectal cancer, breast cancer, cervical cancer, brain cancer, esophageal cancer, and stomach cancer, or a pre-cancerous lesion thereof.

20. The use of claim 19, wherein the tumor is associated with lung cancer or pre-cancerous lesion thereof.

21. The use of claim 12, wherein the subject is a human.

22. The use of claim 12, wherein the tumor exhibits resistance to a chemotherapeutic agent.

23. The use of claim 22, wherein the chemotherapeutic agent is selected from the group consisting of cisplatin and gemcitabine.

24. The use of claim 12, wherein the compound is to be administered with a pharmaceutically acceptable carrier.

25. Use of a compound comprising a CLPTM1L-targeting agent in the manufacture of a medicament for treating or preventing a disease or condition associated with CLPTM1L protein dysfunction, wherein the medicament is to be administered to a cell, tissue, or organ of a subject at risk of, diagnosed as having, or exhibiting a symptom of the disease or condition.

26. The use of claim 25, wherein the CLPTM1L protein dysfunction comprises one or more of pathogenic protein production, pathogenic protein modification, or pathogenic protein function.

27. The use of claim 25, wherein the disease or condition is a tumor, a cancer, or a pre-neoplastic lesion.

28. The use of claim 27, wherein the tumor is a solid tumor selected from the group consisting of glioblastoma, sarcoma, carcinoma, and lymphoma.

29. The use of claim 28, wherein the tumor exhibits resistance to a chemotherapeutic agent.

30. The use of claim 29, wherein the chemotherapeutic agent is selected from the group consisting of cisplatin and gemcitabine

31. The use of claim 25, wherein the CLPTM1L-targeting agent is selected from the group consisting of an antibody, a peptide, and aptamer, or a fragment thereof.

32. The use of claim 25, wherein the CLPTM1L-targeting agent is a monoclonal antibody specific for at least a portion of a CLPTM1L polypeptide.

33. The use of claim 32, wherein the monoclonal antibody is specific to a CLPTM1L polypeptide having one or more of the mutations set forth in Table 2.

34. The use of claim 32, wherein the monoclonal antibody is specific to a peptide having an amino acid sequence selected from the group consisting of SEQ ID NO:4-25.

35. The use of claim 25, wherein the compound is to be administered with a pharmaceutically acceptable carrier.