DESCRIPTION

METHODS AND COMPOSITIONS FOR TUSC2 IMMUNOTHERAPY

[0001] This application claims the benefit of United States Provisional Patent Application No. 62/407,329, filed October 12, 2016, the entirety of which is incorporated herein by reference.

BACKGROUND OF THE INVENTION

1. Field of the Invention

[0002] The present embodiments provided herein relate generally to the fields of molecular biology, immunology and cancer therapy.

2. Description of Related Art

[0003] As the molecular and genetic mechanisms of oncogenesis become better elucidated, the focus of cancer therapy has shifted from the tissue to the genetic level (Bishop, 1991). Mutations in two major classes of genes, oncogenes and tumor suppressor genes (TSGs), play central roles in the oncogenic process. TSGs appear to require homozygous deletion or mutation for inactivation, and restoration of TSG expression is feasible in human tumors (Lowe *et al.,* 2004; Roth, 2006). Homozygous deletions in the 3p21.3 region in lung cancer cell lines and primary lung tumors have led to the identification of multiple genes with tumor suppressor activity from this region (Lerman *et al.,* 2000). These deletions have led to the development of targeted anti-cancer therapies. However, it remains unclear how the efficacy of such therapies could be enhanced.

SUMMARY

[0004] In one aspect, the present disclosure refers to the use of a TUSC2 expression vector in the manufacture of a first medicament and use of an anti-PD1 antibody in the manufacture of a second medicament, wherein the first and second medicaments are to be used in combination therapy to treat lung cancer in a subject. In another aspect, the present disclosure refers to the use of a TUSC2 expression vector in the manufacture of a medicament for use in combination therapy for treating lung cancer in a subject, wherein said medicament is to be administered in combination with an anti- PD1 antibody. In one example, there is disclosed the use of a TUSC2 therapeutic and an immune checkpoint inhibitor in the manufacture of a combination therapy for use in treating a lung cancer. In one example, there is described a method of treating a subject having a cancer comprising administering a tumor suppressor therapy (*e.g.,* a TUSC2 therapy) in conjunction with an immune checkpoint inhibitor. Thus, a method is disclosed for treating a subject having a cancer, wherein the subject is being treated with (or was previously administered) at least one immune checkpoint inhibitor, the method comprising administering a tumor suppressor therapy, such as a TUSC2 therapy, to the subject. For example, a subject to be treated with a TUSC2 therapy can be a subject who was administered an immune checkpoint inhibitor less that one hour, 6 hours, 12 hours, 1 day, 3 days, one week or two weeks before administration of the TUSC2 therapy. As used herein, a TUSC2 therapy can be any

CLAIMS

What Is Claimed Is:

1. Use of a TUSC2 expression vector in the manufacture of a first medicament and use of an anti-PD1 antibody in the manufacture of a second medicament, wherein the first and second medicaments are to be used in combination therapy to treat lung cancer in a subject.

2. Use of a TUSC2 expression vector in the manufacture of a medicament for use in combination therapy for treating lung cancer in a subject, wherein said medicament is to be administered in combination with an anti- PD1 antibody.

3. The use of any one of claims 1 or 2, wherein the anti- PD1 antibody is to be administered to the subject before the TUSC2 expression vector.

4. The use of any one of claims 1 or 2, wherein the anti- PD1 antibody is to be administered to the subject after or concomitantly with the TUSC2 expression vector.

5. The use of any one of claims 1 or 2, wherein the subject had been administered the anti-PD1 antibody no more than two weeks before the TUSC2 expression vector.

6. The use of any one of claims 1 or 2, wherein the subject has been or is to be treated with two immune checkpoint inhibitors.

7. The use of claim 6, wherein the two immune checkpoint inhibitors are an anti-PD1 antibody and an anti-CTL4 antibody.

8. The use of any one of claims 1 or 2, wherein the TUSC2 expression vector is plasmid DNA.

9. The use of claim 8, wherein the plasmid is pLJ143/KGB2/FUS1.

10. The use of any one of claims 1 or 2, wherein the TUSC2 expression vector is provided in a liposome.

11. The use of claim 10, wherein the liposome is a N-[1-(2,3-dioleoyloxy)propyl]-N,N,N-trimethylammonium chloride (DOTAP):cholesterol liposome.

12. The use of claim 11, wherein the DOTAP:cholesterol ratio is between 1.5:1 and 1:1.5.

13. The use of claim 11, wherein the DOTAP:cholesterol ratio is about 10:9.

14. The use of claim 11, wherein the TUSC2 expression vector and DOTAP:cholesterol liposome are to be administered in a dose of from 0.01 mg/kg to 0.10 mg/kg.

15. The use of any one of claims 1 or 2, wherein the TUSC2 expression vector is to be administered two or more times.

16. The use of any one of claims 1 or 2, further comprising an anti-inflammatory agent to be administered.

17. The use of any one of claims 1 or 2, further comprising a TUSC2 polypeptide to be administered.

18. The use of claim 17, wherein the TUSC2 polypeptide is myristoylated.

19. The use of claim 17, wherein the TUSC2 polypeptide is comprised in a nanoparticle.

20. The use of claim 19, wherein the nanoparticle is a lipid-based nanoparticle, a superparamagnetic nanoparticle, a nanoshell, a semiconductor nanocrystal, a quantum dot, a polymer-based nanoparticle, a silicon-based nanoparticle, a silica-based nanoparticle, a metal-based nanoparticle, a fullerene or a nanotube.

21. The use of any one of claims 1 or 2, further comprising a further anti-cancer therapy is to be administered to the subject.

22. The use of claim 21, wherein the further anti-cancer therapy is chemotherapy, radiotherapy, gene therapy, surgery, hormonal therapy, anti-angiogenic therapy or cytokine therapy.

23. The use of claim 22, wherein the further anti-cancer therapy is an EGFR inhibitor.

24. The use of any one of claims 1 or 2, wherein the lung cancer is a non-small cell lung cancer.

25. The use of any one of claims 1 or 2, wherein the cancer is a metastatic lung cancer.

26. The use of any one of claims 1 or 2, wherein the cancer is resistant to a least a first chemotherapy.

27. The use of claim 26, wherein the cancer is resistant to a platinum-based chemotherapy.

28. The use of any one of claims 1 or 2, wherein the TUSC2 expression vector and the anti-PD1 antibody to be administered result in an increase of NK and/or $CD8^+$ T cell density in the tumor.

29. The use of claim 28, wherein the CD8+ T cell density increases by at least 3-fold.

30. The use of any one of claims 1 or 2, wherein the TUSC2 expression vector and the anti-PD1 antibody to be administered result in CcL3, CcL4, CcL21a, and/or CcL19 serum levels.

31. The use of claim 23, wherein the EGFR inhibitor is a tyrosine kinase inhibitor.

32. The use of claim 23, wherein the EGFR inhibitor is an EGFR binding antibody or aptamer.

33. The use of claim 23, wherein the EGFR inhibitor is gefitinib, erlotinib, cetuximab, matuzumab, panitumumab, AEE788; CI-1033, HKI-272, HKI-357 or EKB-569.