similarities between aerobic bacteria and mitochondria, certain classes of antibiotics or compounds having antibiotic activity can inhibit mitochondrial protein translation as an off-target side-effect.

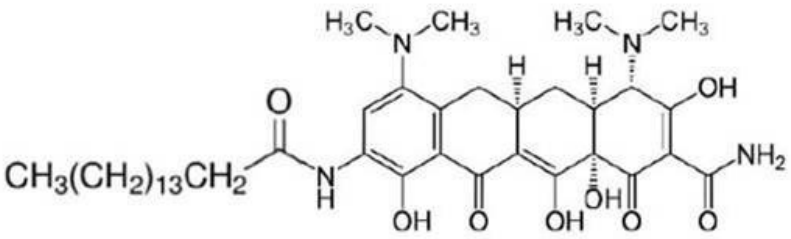
SUMMARY

[0005] In view of the foregoing background, it is an object of this disclosure to demonstrate that existing antibiotics having intrinsic anti-mitochondrial properties can be chemically modified to target the mitochondria and thus can be used to eradicate CSCs. In one aspect, there is provided an antimitoscin comprising an antibiotic having intrinsic anti-mitochondrial properties chemically modified with a membrane targeting signal comprising a fatty acid moiety, wherein the antibiotic is selected from doxycycline, tigecycline, minocycline, chlortetracycline, oxytetracycline, demeclocycline, lymecycline, meclocycline, methacycline, rolitetracycline, omadacycline, and sarecycline. In another aspect, there is provided use of a pharmaceutically effective amount of an antimitoscin and a pharmaceutically acceptable carrier in the manufacture of a medicament for treating cancer, the antimitoscin comprising an antibiotic having intrinsic anti-mitochondrial properties chemically modified with a membrane targeting signal comprising a fatty acid moiety, wherein the antibiotic is selected from doxycycline, tigecycline, minocycline, chlortetracycline, oxytetracycline, demeclocycline, lymecycline, meclocycline, methacycline, rolitetracycline, omadacycline, and sarecycline. In another aspect, there is provided use of a pharmaceutical composition in the manufacture of a medicament for treating cancer, said pharmaceutical composition containing, as the active ingredient, at least one antimitoscin, the antimitoscin comprising an antibiotic having intrinsic anti-mitochondrial properties chemically modified with a membrane targeting signal comprising a fatty acid moiety, wherein the antibiotic is selected from doxycycline, tigecycline, minocycline, chlortetracycline, oxytetracycline, demeclocycline, lymecycline, meclocycline, methacycline, rolitetracycline, omadacycline, and sarecycline. In a further aspect, there is provided an antimitoscin synthesis method comprising: chemically modifying an antibiotic having anti-cancer properties with a membrane targeting signal comprising a fatty acid, wherein the antibiotic is selected from doxycycline, tigecycline, minocycline, chlortetracycline, oxytetracycline, demeclocycline, lymecycline, meclocycline, methacycline, rolitetracycline, omadacycline, and sarecycline. In a further aspect, there is provided a method for improving the anti-cancer properties of an antibiotic, the method comprising: chemically modifying an antibiotic having anti-cancer properties with a membrane targeting signal comprising a fatty acid, wherein the antibiotic is selected from doxycycline, tigecycline, minocycline, chlortetracycline, oxytetracycline, demeclocycline, lymecycline, meclocycline, methacycline, rolitetracycline, omadacycline, and sarecycline. In a further aspect, there is provided a method for monitoring the effectiveness of an antimitoscin therapy, the method comprising: determining the level of at least one CSC marker in a tissue sample obtained from a patient; and classifying the antimitoscin therapy as effective if the sample is determined to have a decreased level of at least one CSC marker relative to a threshold level, wherein the antimitoscin is as disclosed herein.

CLAIMS

What is claimed is:

1. An antimitoscin comprising an antibiotic having intrinsic anti-mitochondrial properties chemically modified with a membrane targeting signal comprising a fatty acid moiety, wherein the antibiotic is selected from doxycycline, tigecycline, minocycline, chlortetracycline, oxytetracycline, demeclocycline, lymecycline, meclocycline, methacycline, rolitetracycline, omadacycline, and sarecycline.

2. The antimitoscin of claim 1, wherein the antimitoscin comprises the formula: , or pharmaceutically acceptable salts thereof.

3. The antimitoscin of claim 1, wherein the antibiotic is doxycycline or tigecycline.

4. The antimitoscin of claim 1, wherein the membrane targeting signal is one of palmitic acid, stearic acid, myristic acid, and oleic acid.

5. The antimitoscin of claim 3, wherein the membrane targeting signal is one of palmitic acid, stearic acid, myristic acid, and oleic acid.

6. The antimitoscin of claim 1, wherein the antimitoscin possesses anti-cancer activity.

7. The antimitoscin of claim 1, wherein the antimitoscin binds to the large sub-unit of the mitochondrial ribosome.

8. The antimitoscin of claim 1, wherein the antimitoscin binds to the small sub-unit of the mitochondrial ribosome.

9. The antimitoscin of claim 1, wherein the antimitoscin binds to at least one of the large sub-unit of the mitochondrial ribosome or the small sub-unit of the mitochondrial ribosome.

10. The antimitoscin of claim 1, wherein the antimitoscin binds to a mitochondrial membrane.

11. The antimitoscin of claim 1, wherein the antimitoscin possesses radiosensitizing activity.

12. The antimitoscin of claim 1, wherein the antimitoscin possesses photosensitizing activity.

13. The antimitoscin of claim 1, wherein the antimitoscin sensitizes cancer cells to chemotherapeutic agents.

14. The antimitoscin of claim 1, wherein the antimitoscin sensitizes cancer cells to natural substances.

15. The antimitoscin of claim 1, wherein the antimitoscin sensitizes cancer cells to caloric restriction.

16. Use of a pharmaceutically effective amount of an antimitoscin and a pharmaceutically acceptable carrier in the manufacture of a medicament for treating cancer, the antimitoscin comprising an antibiotic having intrinsic anti-mitochondrial properties chemically modified with a membrane targeting signal comprising a fatty acid moiety, wherein the antibiotic is selected from doxycycline, tigecycline, minocycline, chlortetracycline, oxytetracycline, demeclocycline, lymecycline, meclocycline, methacycline, rolitetracycline, omadacycline, and sarecycline.

17. Use of a pharmaceutical composition in the manufacture of a medicament for treating cancer, said pharmaceutical composition containing, as the active ingredient, at least one antimitoscin, the antimitoscin comprising an antibiotic having intrinsic anti-mitochondrial properties chemically modified with a membrane targeting signal comprising a fatty acid moiety, wherein the antibiotic is selected from doxycycline, tigecycline, minocycline, chlortetracycline,

oxytetracycline, demeclocycline, lymecycline, meclocycline, methacycline, rolitetracycline, omadacycline, and sarecycline.

18. The use of claim 17, wherein the pharmaceutical composition comprises a plurality of said antimitoscins.

19. An antimitoscin synthesis method comprising:

chemically modifying an antibiotic having anti-cancer properties with a membrane targeting signal comprising a fatty acid, wherein the antibiotic is selected from doxycycline, tigecycline, minocycline, chlortetracycline, oxytetracycline, demeclocycline, lymecycline, meclocycline, methacycline, rolitetracycline, omadacycline, and sarecycline.

20. The method of claim 19, wherein the antibiotic is one of doxycycline, tigecycline and minocycline.

21. The method of claim 19, wherein the fatty acid is selected from palmitic acid, stearic acid, myristic acid, and oleic acid.

22. The method of claim 20, wherein the antibiotic is selected from doxycycline, tigecycline and minocycline, and the fatty acid is selected from palmitic acid, stearic acid, myristic acid, and oleic acid.

23. A method for improving the anti-cancer properties of an antibiotic, the method comprising:

chemically modifying an antibiotic having anti-cancer properties with a membrane targeting signal comprising a fatty acid, wherein the antibiotic is selected from doxycycline, tigecycline, minocycline, chlortetracycline, oxytetracycline, demeclocycline, lymecycline, meclocycline, methacycline, rolitetracycline, omadacycline, and sarecycline.

24. The method of claim 23, wherein the antibiotic is selected from doxycycline, tigecycline and minocycline.

25. The method of claim 23, wherein the fatty acid is selected from palmitic acid, stearic acid, myristic acid, and oleic acid.

26. The method of claim 24, wherein the antibiotic is selected from doxycycline, tigecycline and minocycline, and the fatty acid is selected from palmitic acid, stearic acid, myristic acid, and oleic acid.

27. A method for monitoring the effectiveness of an antimitoscin therapy, the method comprising:

determining the level of at least one CSC (cancer stem cell) marker in a tissue sample obtained from a patient;

and classifying the antimitoscin therapy as effective if the sample is determined to have a decreased level of at least one CSC marker relative to a threshold level,

wherein the antimitoscin is as set forth in any one of claims 1 to 15.

28. The method of claim 27, wherein the CSC marker is at least one of CD44, Sox2, Nanog, Oct 4, MYC, and ALDH.