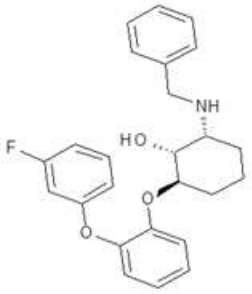
therapies to treat drug-resistance that is characteristic of both tumor recurrence and infectious disease, and such therapies may have the additional benefit of slowing the aging process.

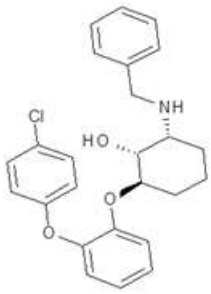
SUMMARY

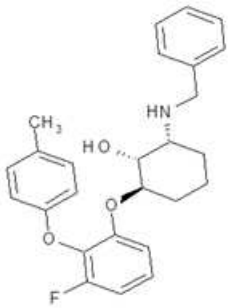
[0006] In view of the foregoing background, it is therefore an object of this disclosure to demonstrate that mitochondrial biogenesis plays a critical role in the propagation and maintenance of many cancers. It is also an object of this disclosure to present methods for identifying mitochondrial inhibitors that bind to the mitochondrial ribosome (large sub-unit or small sub-unit) and have anti-cancer and antibiotic properties. It is also an object of this disclosure to identify mitochondrial inhibitors and groups thereof and having anti-cancer and antibiotic properties. It is also an object of this disclosure to identify classes of mitochondrial inhibitors having anti-aging properties. It is also an object of this disclosure to identify classes of mitochondrial inhibitors that function as radiosensitizers and photosensitizers.

[0007] The present disclosure relates to mitochondrial inhibitor compounds that have anti-cancer and antimicrobial activity, radiosensitizing and photosensitizing effects, as well as anti-aging effects. The term “mitoriboscins” broadly refers to mitoribosome-targeted therapeutics having anti-cancer and antibiotic properties. These compounds bind to either the large sub-unit or the small sub-unit of the mitoribosome (or in some instances, both) and inhibit mitochondrial biogenesis. The present disclosure further relates to methods of identifying mitoriboscins, methods of making such mitoriboscins, and methods of using mitoriboscins for therapeutic purposes.

[0007a] In one aspect, the present disclosure refers to the use of a mitoriboscin and a pharmaceutically acceptable carrier in the manufacture of a medicament for treating cancer, wherein the mitoriboscin comprises the general formula of at least one of:

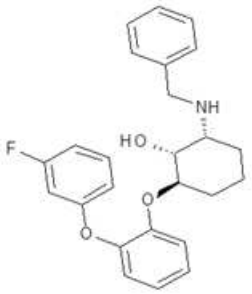


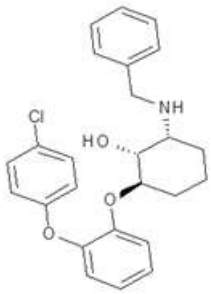
, 

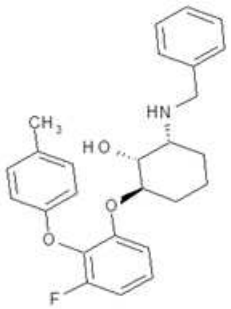
, and 

, or a pharmaceutically acceptable salt thereof.

[0007b] In another aspect, the present disclosure refers to the use of a mitoriboscin and a pharmaceutically acceptable carrier in the manufacture of a medicament for treating microbial infection or a pathogenic yeast infection, wherein the mitoriboscin comprises the general formula of at least one of:

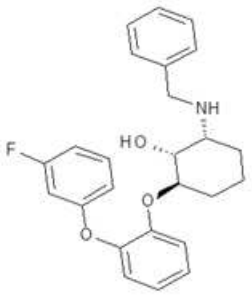


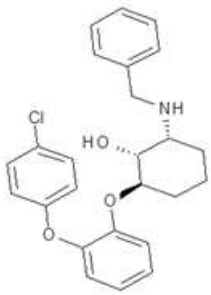
, 

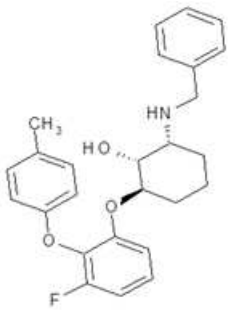
, and 

, or a pharmaceutically acceptable salt thereof.

[0007c] In a further aspect, the present disclosure refers to a pharmaceutical composition for use in therapy containing, as the active ingredient, at least one mitoriboscin, wherein the mitoriboscin comprises the general formula of at least one of:

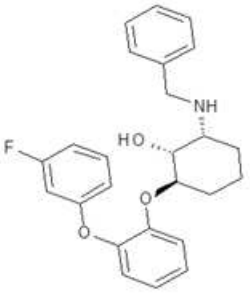


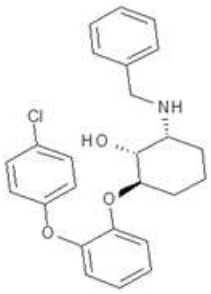
, 

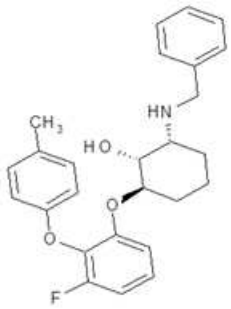
, and 

, or a pharmaceutically acceptable salt thereof.

[0007d] In yet another aspect, the present disclosure refers to a non-therapeutic method of treating an age-related condition or aging, the method comprising administration of a mitoriboscin and a pharmaceutically acceptable carrier, wherein the mitoriboscin comprises the general formula of at least one of:



, 

, and 

, or a pharmaceutically acceptable salt thereof.

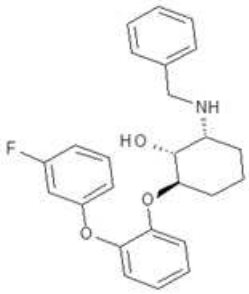
[0008] The inventors analyzed phenotypic properties of cancer stem cells (CSCs) that could be targeted across a wide range of cancer types, and identified a strict dependence of CSCs on mitochondrial biogenesis for the clonal expansion and survival of a CSC. Previous work by the inventors demonstrated that different classes of FDA-approved antibiotics, and in particular tetracyclines such as doxycycline and erythromycin, have an off-target effect of inhibiting mitochondrial biogenesis. As a result, such compounds could have efficacy for eradicating CSCs. However, these common antibiotics were not designed to target the mitoribosome, and therefore have limited anti-cancer properties. Under the present approach, the inventors have identified compounds that target the mitochondrial ribosome, or mitoribosome, and inhibit mitochondrial biogenesis. These mitoribosome-targeting compounds – mitoriboscins – therefore have highly potent anticancer properties, among other advantageous properties.

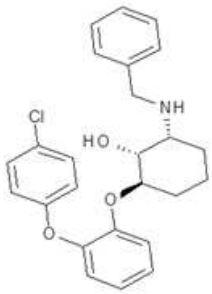
[0009] Given the role of mitochondrial biogenesis in cell propagation, mitochondrial inhibitors as identified under the present approach provide an entirely new class of cancer therapy. In addition to their potential use as cancer therapies, mitoriboscins serve as useful broad-spectrum antibiotics. The endo-symbiotic theory of mitochondrial evolution theorizes that mitochondrial organelles evolved from engulfed aerobic bacteria following millions of years of symbiosis and adaptation. The evolutionary history of mitochondrial organelles suggests that compounds that target mitochondrial protein translation in cancer cells also possess anti-

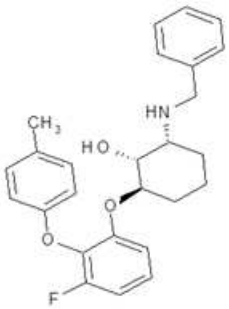
CLAIMS

What is claimed is:

1. Use of a mitoriboscin and a pharmaceutically acceptable carrier in the manufacture of a medicament for treating cancer, wherein the mitoriboscin comprises the general formula of at least one of:

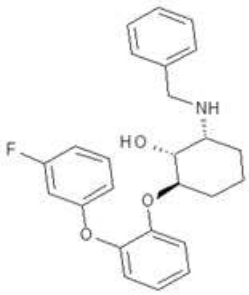


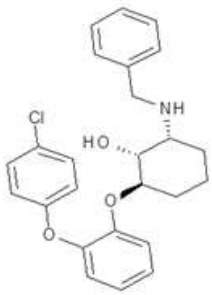
, 

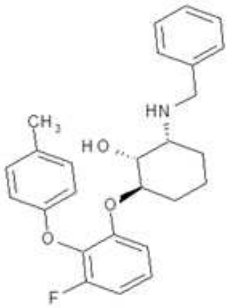
, and 

, or a pharmaceutically acceptable salt thereof.

2. Use of a mitoriboscin and a pharmaceutically acceptable carrier in the manufacture of a medicament for treating microbial infection or a pathogenic yeast infection, wherein the mitoriboscin comprises the general formula of at least one of:

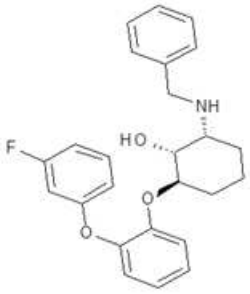


, 

, and 

, or a pharmaceutically acceptable salt thereof.

3. A pharmaceutical composition for use in therapy containing, as the active ingredient, at least one mitoriboscin, wherein the mitoriboscin comprises the general formula of at least one of:



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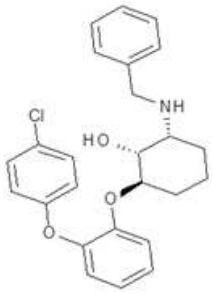

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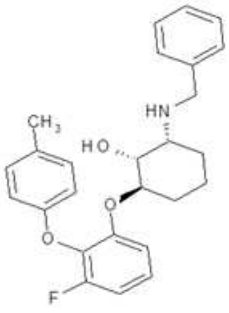


, or a pharmaceutically acceptable salt thereof.

4. The use of any one of claims 1 to 2 or the pharmaceutical composition of claim 3, wherein the mitoriboscin possesses anti-aging activity, or radiosensitizing activity, or photosensitizing activity.

5. The use of any one of claims 1 to 2 or the pharmaceutical composition of claim 3, wherein the mitoriboscin sensitizes cancer cells to chemotherapeutic agents.

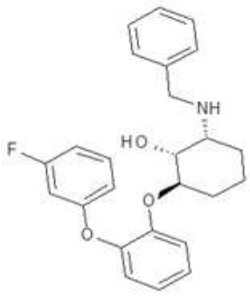
6. The use of any one of claims 1 to 2 or the pharmaceutical composition of claim 3, wherein the mitoriboscin sensitizes cancer cells to natural substances.

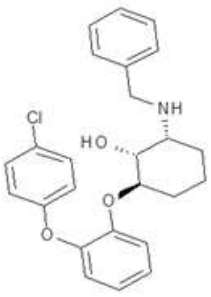
7. The use of any one of claims 1 to 2 or the pharmaceutical composition of claim 3, wherein the mitoriboscin sensitizes cancer cells to caloric restriction.

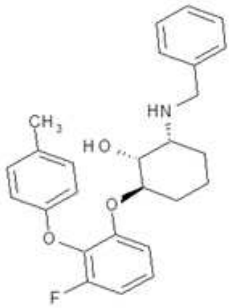
8. The use of any one of claims 1 to 2 or the pharmaceutical composition of claim 3, wherein the mitoriboscin binds to the large sub-unit of the mitochondrial ribosome.

9. The use of any one of claims 1 to 2 or the pharmaceutical composition of claim 3, wherein the mitoriboscin binds to the small sub-unit of the mitochondrial ribosome.

10. A non-therapeutic method of treating an age-related condition or aging, the method comprising administration of a mitoriboscin and a pharmaceutically acceptable carrier, wherein the mitoriboscin comprises the general formula of at least one of:



, 

, and 

, or a pharmaceutically acceptable salt thereof.