US 20210052630A1

(19) **United States**

(12) **Patent Application Publication** (10) **Pub. No.: US 2021/0052630 A1**

JIANG et al. (43) **Pub. Date: Feb. 25, 2021**

(54) **METHODS AND COMPOSITIONS FOR PREVENTING OR TREATING HEART DISEASE**

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(21) Appl. No.: **16/999,051**

(22) Filed: **Aug. 20, 2020**

(30) **Foreign Application Priority Data**

Aug. 23, 2019 (CN) 201910784150.9

Publication Classification

(51) **Int. Cl.**

A61K 31/7105	(2006.01)
A61K 47/54	(2006.01)
A61P 9/00	(2006.01)

(52) **U.S. Cl.**

CPC ***A61K 31/7105*** (2013.01); ***A61P 9/00*** (2018.01); ***A61K 47/543*** (2017.08)

(57) **ABSTRACT**

Application of transfer RNA Molecules and their derived fragments for prevention or treatment of heart disease. The present invention provides a method of preventing or treating a subject suffering from heart diseases comprising administration of transfer RNA molecules and fragments derived from transfer RNA molecules or its functional variants or homologous to the subject, wherein the RNA molecules isolated from or derived from a plant of the genus *Panax*. The present invention also provides a pharmaceutical composition for the prevention or treatment of heart diseases comprising said effective amount of RNA molecule and a pharmaceutically tolerable vector, virus or excipient. The present invention provides a method for the prevention or treatment of a subject suffering from a heart disease. It is found that transfer RNA molecules from ginseng are particularly effective in the treatment of heart diseases, and also have a restorative effect on the myocardial cytoskeleton after ischemia-reperfusion injury.

Specification includes a Sequence Listing.

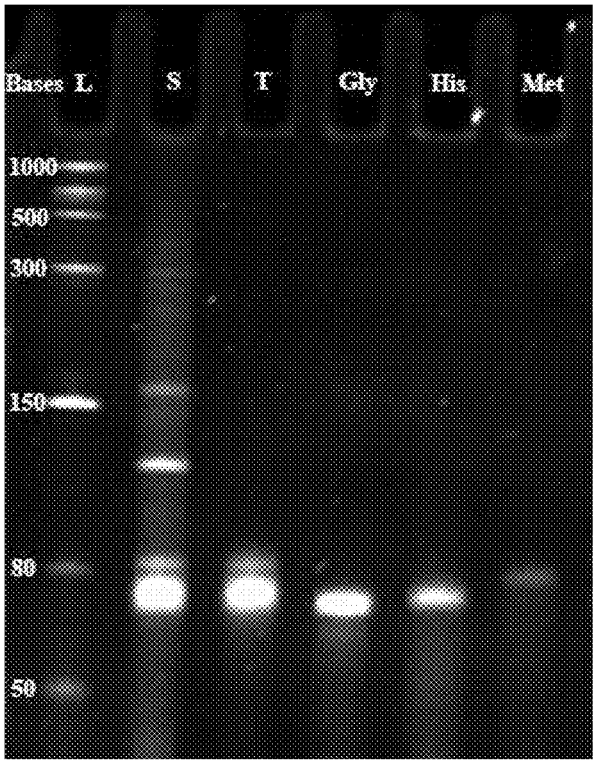
Bases L
S
T
Gly
His
Met
1000
500
300
150
80
50

Fig.1

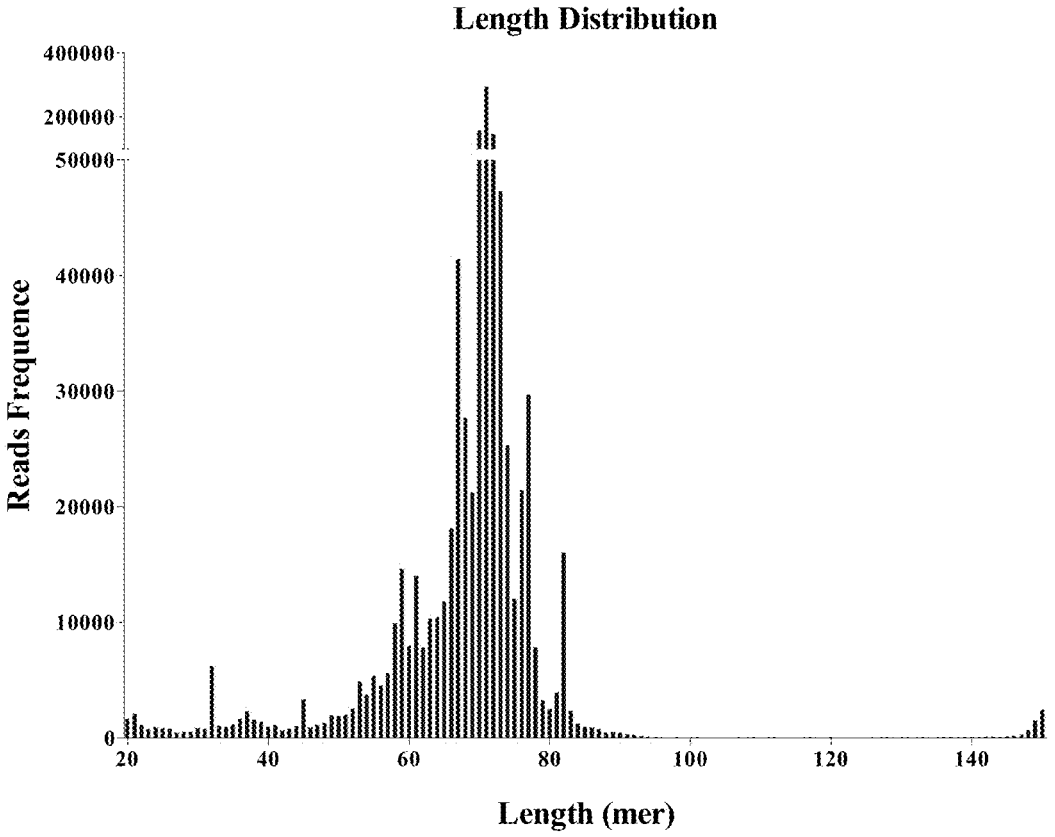
Length Distribution
Reads Frequence
400000
200000
50000
40000
30000
20000
10000
0
20
40
60
80
100
120
140
Length (mer)

Fig.2

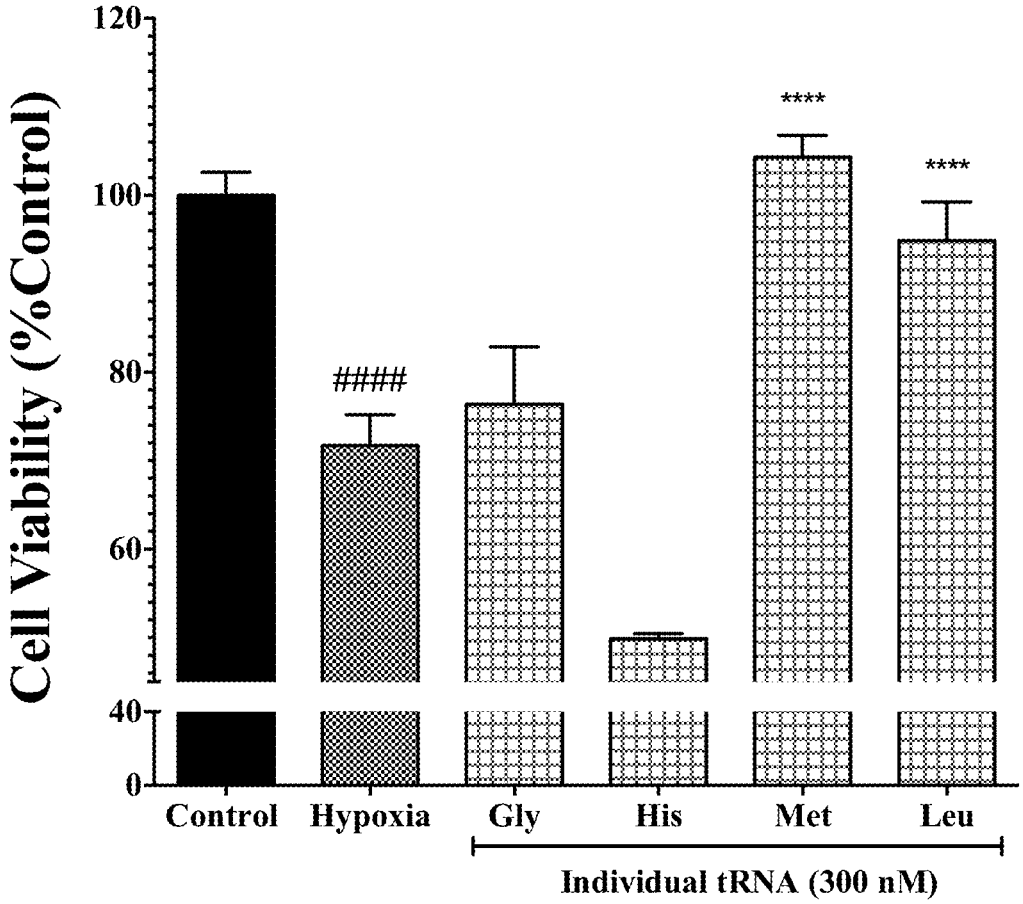
Cell Viability (%Control)
120
100
80
60
40
0
####
****
****
Control
Hypoxia
Gly
His
Met
Leu
Individual tRNA (300 nM)

Fig.3A

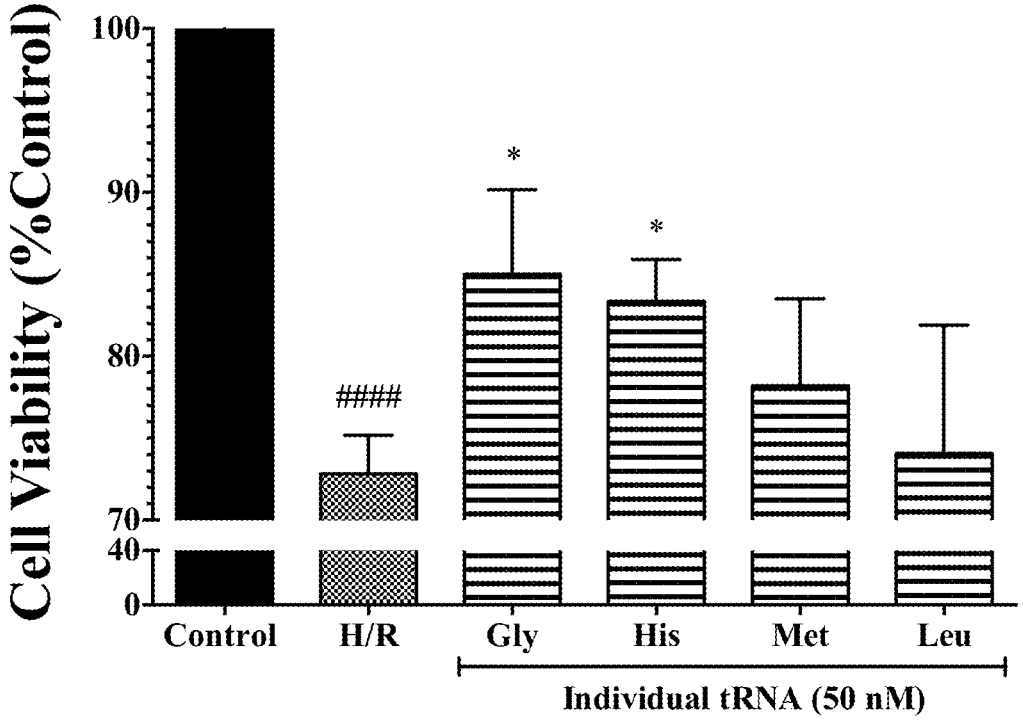
Cell Viability (%Control)
100
90
80
70
40
0
####
*
*
Control
H/R
Gly
His
Met
Leu
Individual tRNA (50 nM)

Fig.3B

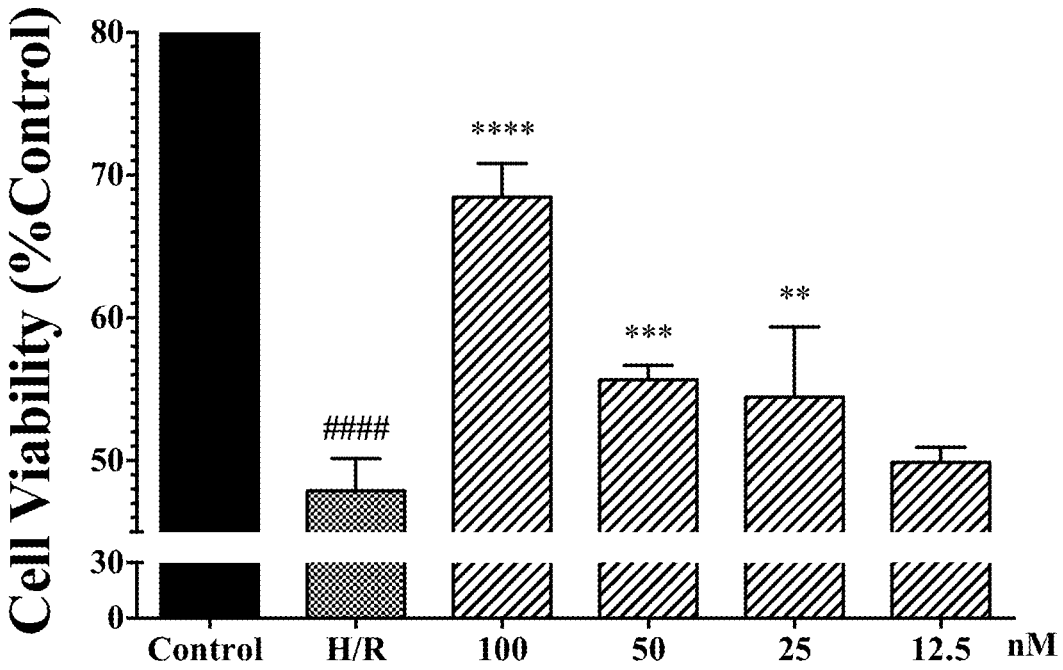
Cell Viability (%Control)
80
70
60
50
30
0
****
###
***
**
Control
H/R
100
50
25
12.5
nM

Fig.4A

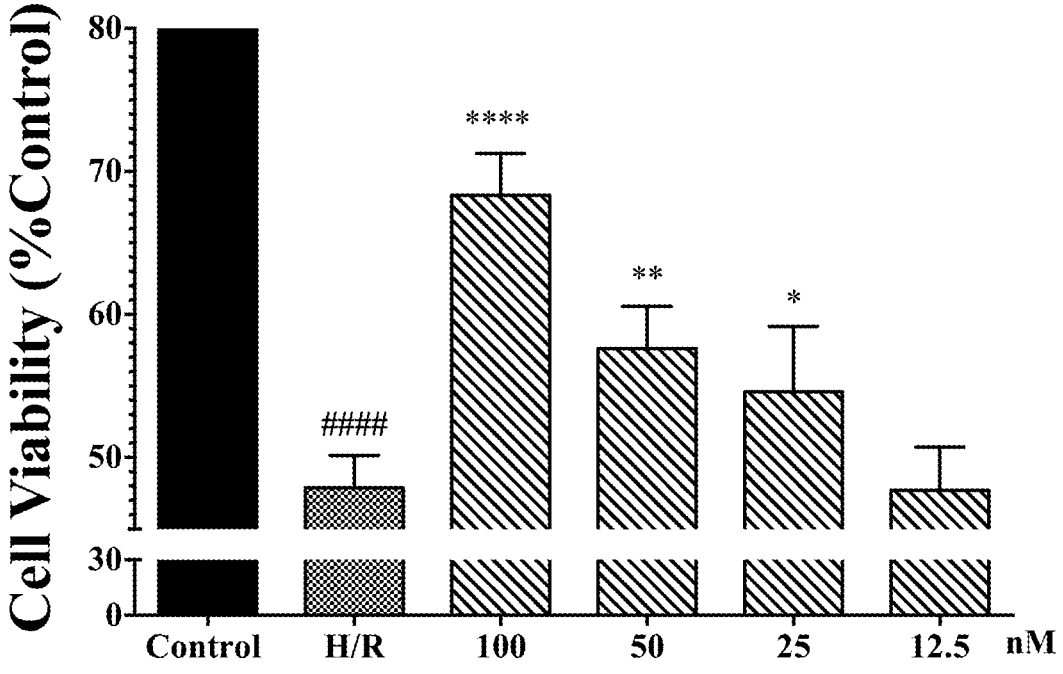
Cell Viability (%Control)
80
70
60
50
30
0
****
###
**
*
Control
H/R
100
50
25
12.5
nM

Fig.4B

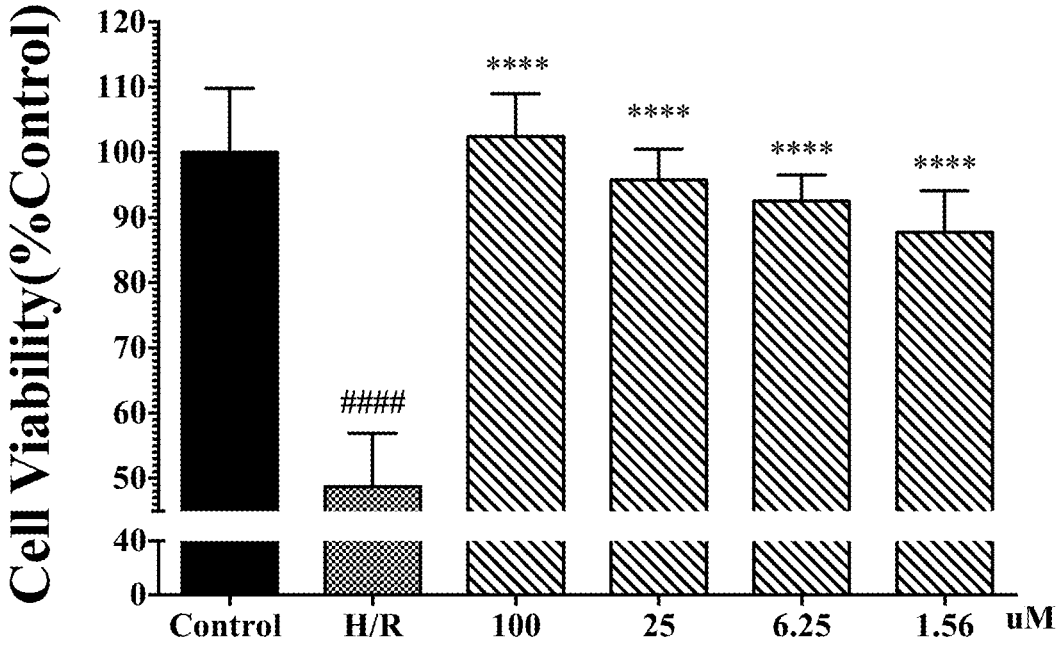
Cell Viability(%Control)
120
110
100
90
80
70
60
50
40
0
****
****
****
****
####
Control
H/R
100
25
6.25
1.56
uM

Fig.4C

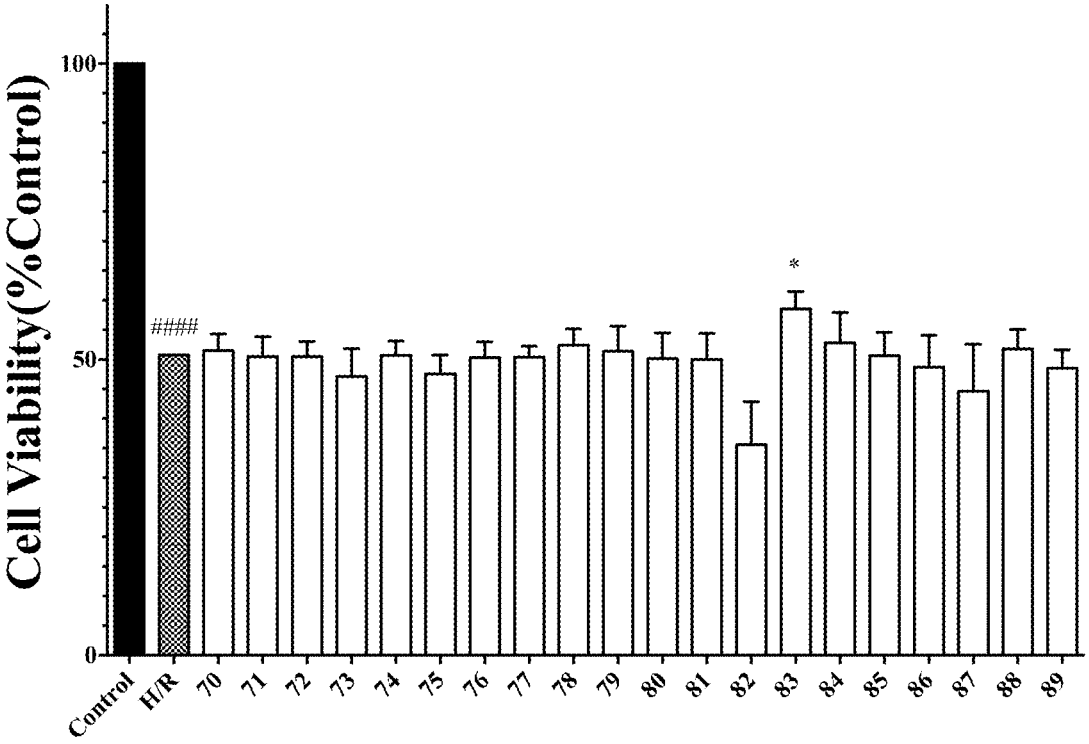
Cell Viability(%Control)
100
50
0
*
####
Control
H/R
70
71
72
73
74
75
76
77
78
79
80
81
82
83
84
85
86
87
88
89

Fig.5A

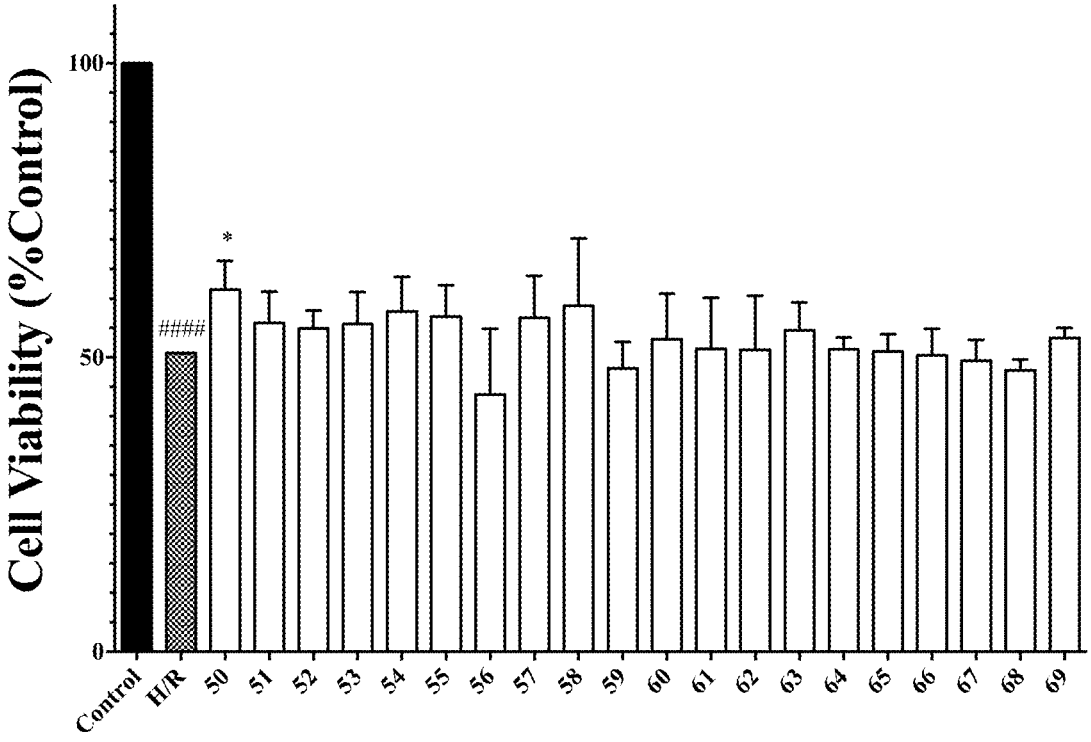
Cell Viability (%Control)
100
50
0
*
#####
Control
H/R
50
51
52
53
54
55
56
57
58
59
60
61
62
63
64
65
66
67
68
69

Fig.5B

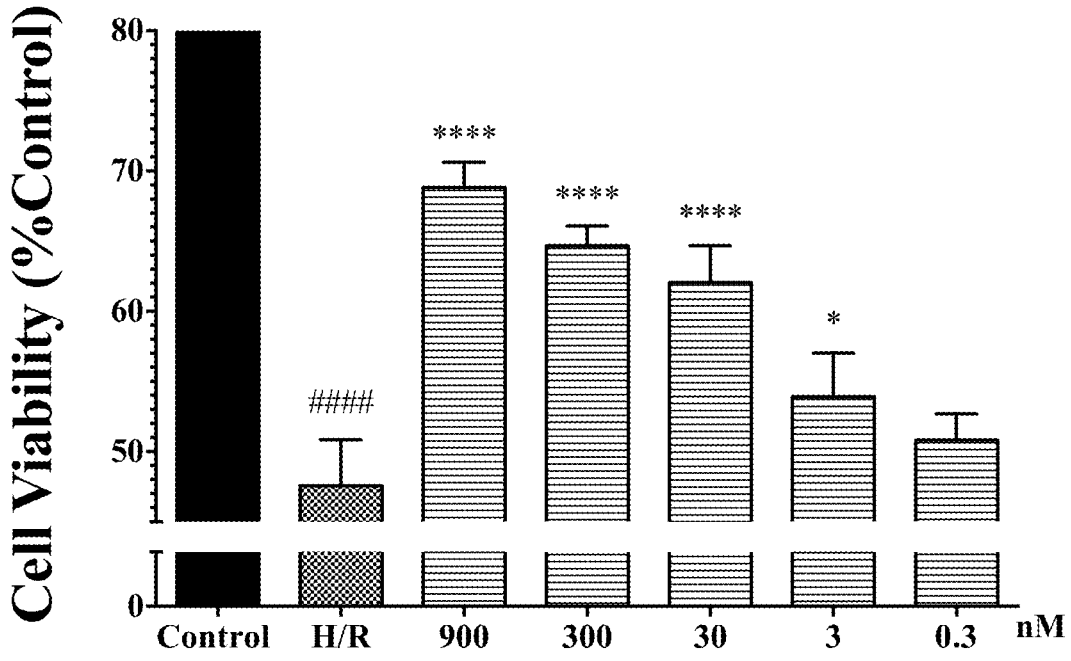
Cell Viability (%Control)
80
70
60
50
0
****
****
****
*
#####
Control
H/R
900
300
30
3
0.3
nM

Fig.6A

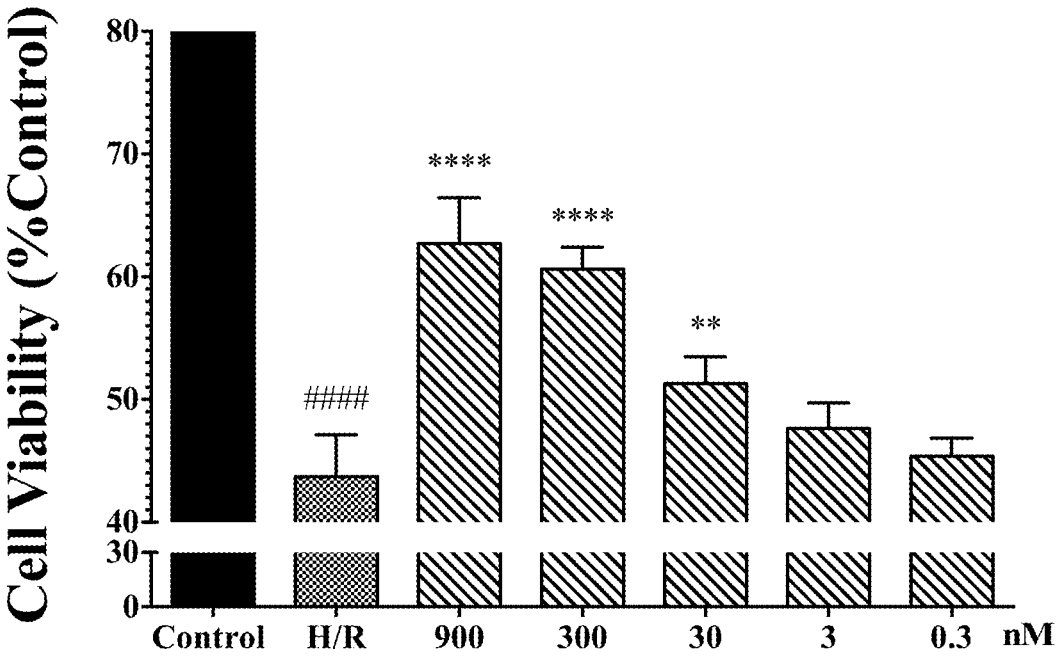
Cell Viability (%Control)
80
70
60
50
40
30
0
****
****
**
####
Control
H/R
900
300
30
3
0.3
nM

Fig.6B

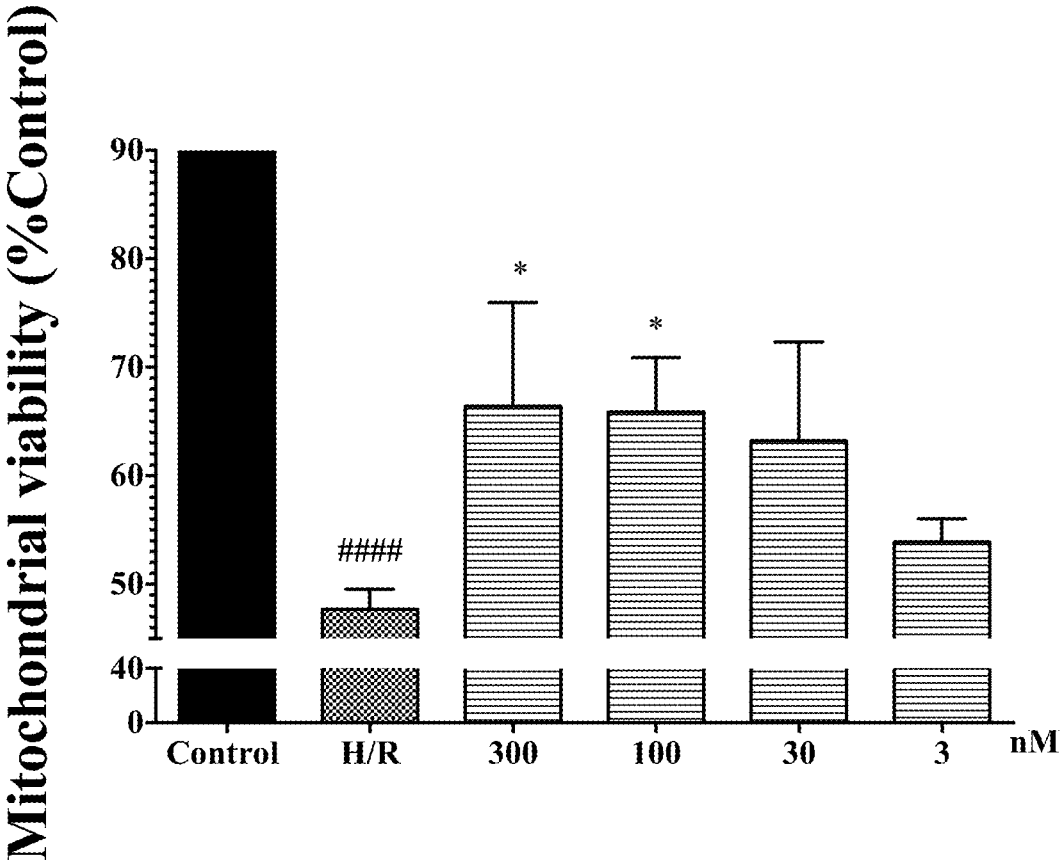
Mitochondrial viability (%Control)
90
80
70
60
50
40
0
*
*
####
Control
H/R
300
100
30
3
nM

Fig.7A

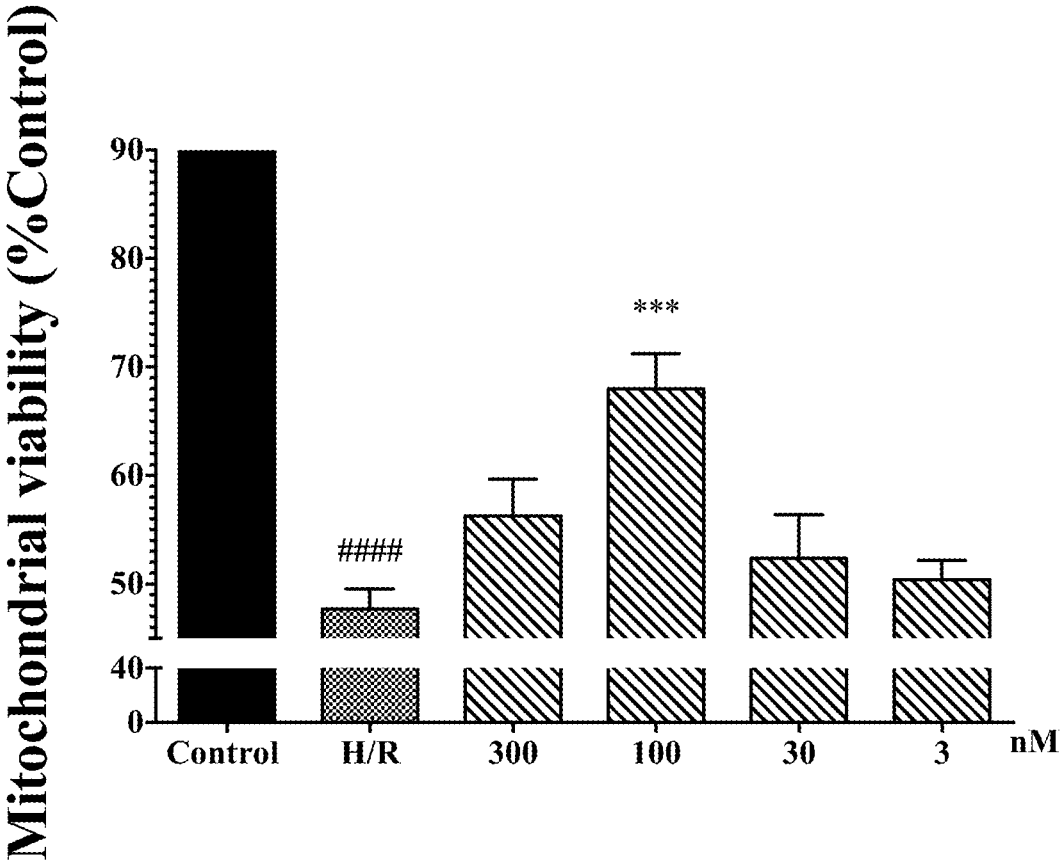
Mitochondrial viability (%Control)
90
80
70
60
50
40
0
####
***
Control
H/R
300
100
30
3
nM

Fig.7B

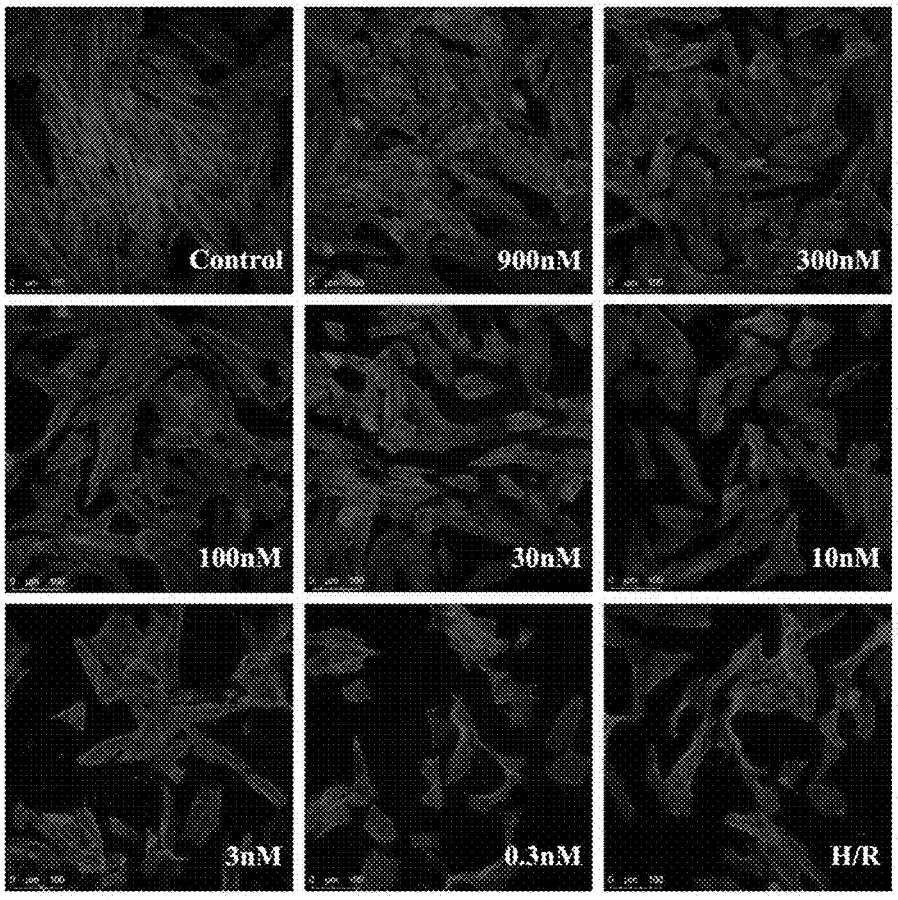

Fig.8A

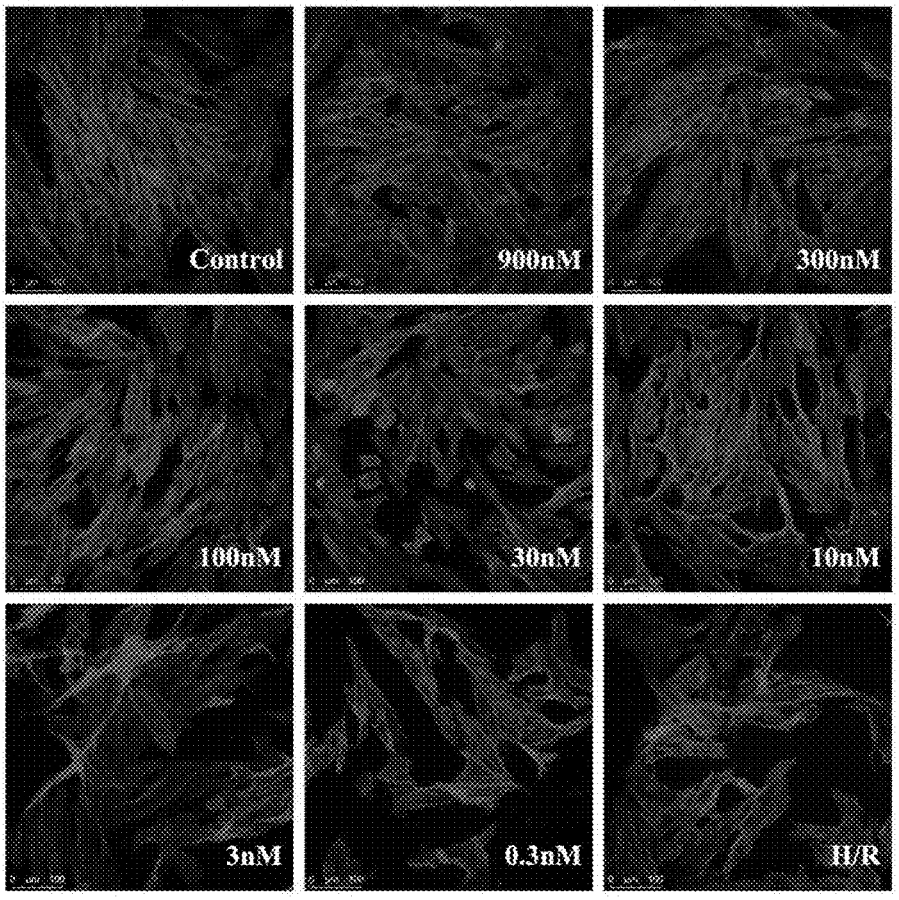
Control
900nM
300nM
100nM
30nM
10nM
3nM
0.3nM
H/R

Fig.8B

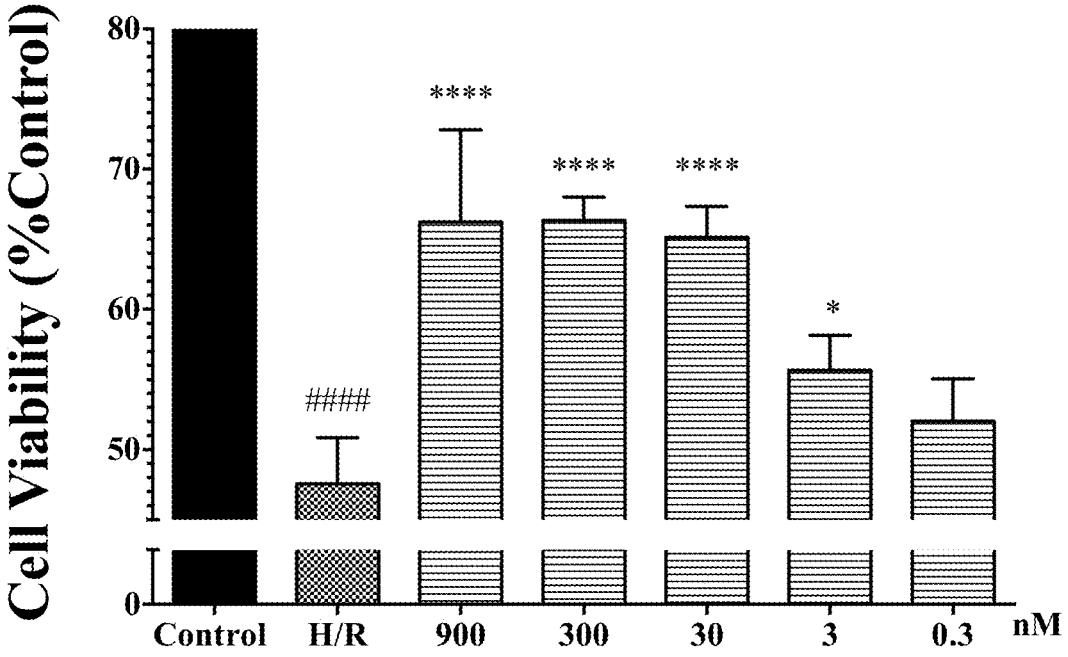
Cell Viability (%Control)
80
70
60
50
0
****
****
****
*
####
Control
H/R
900
300
30
3
0.3
nM

Fig.9A

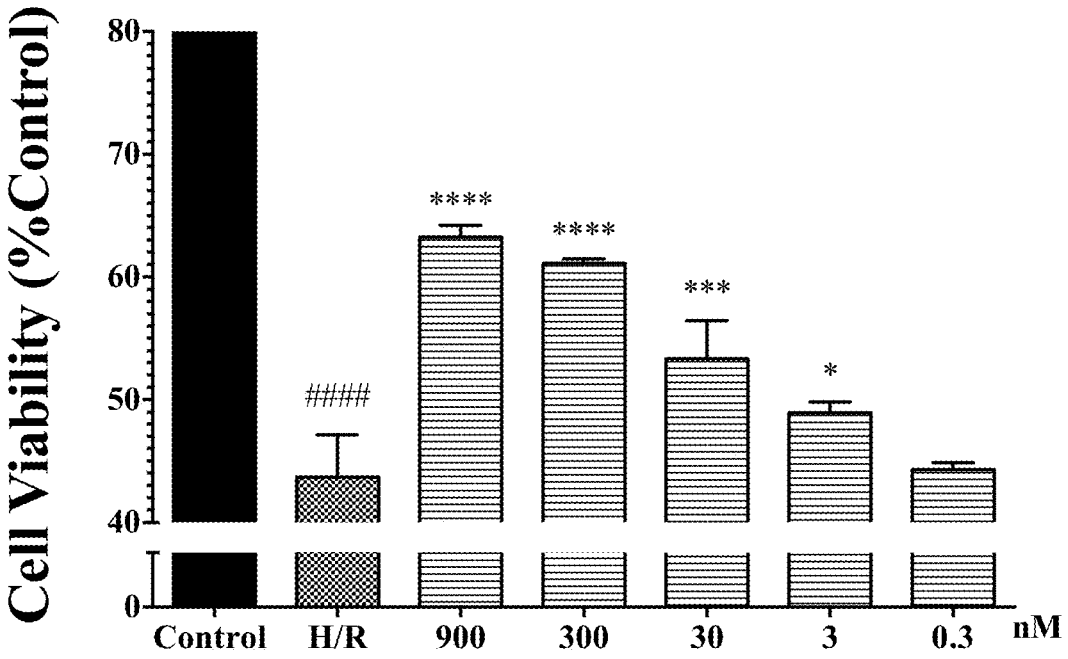

Fig.9B

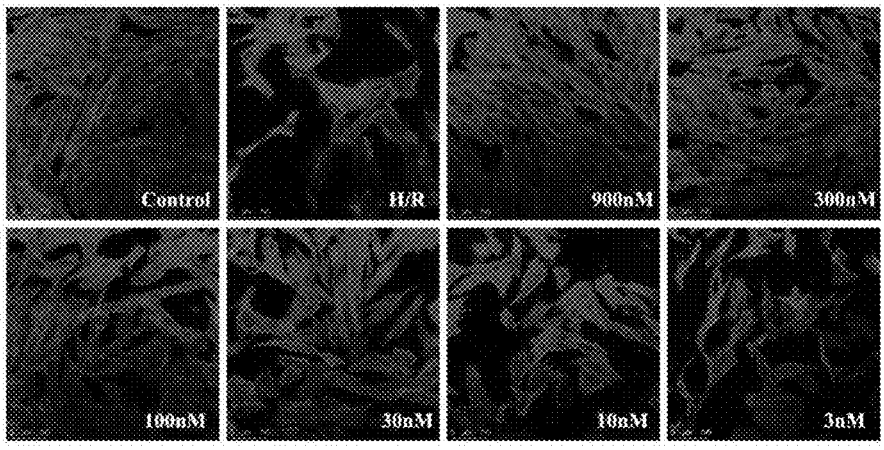

Fig.10A

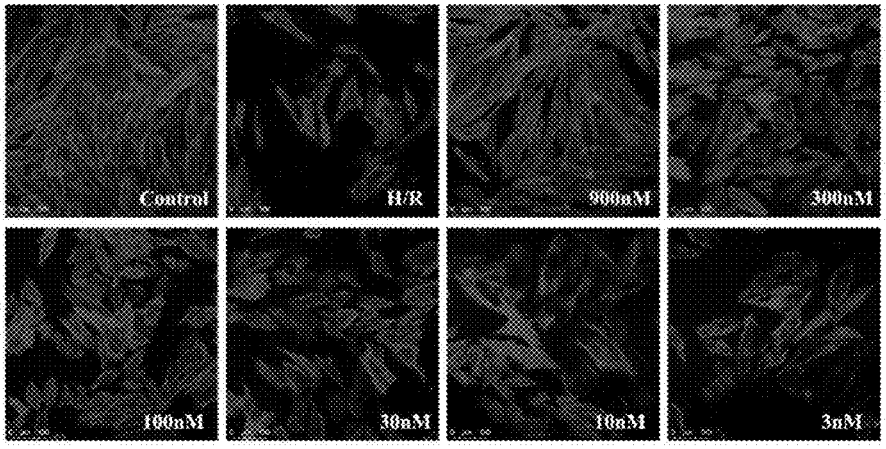

Fig.10B

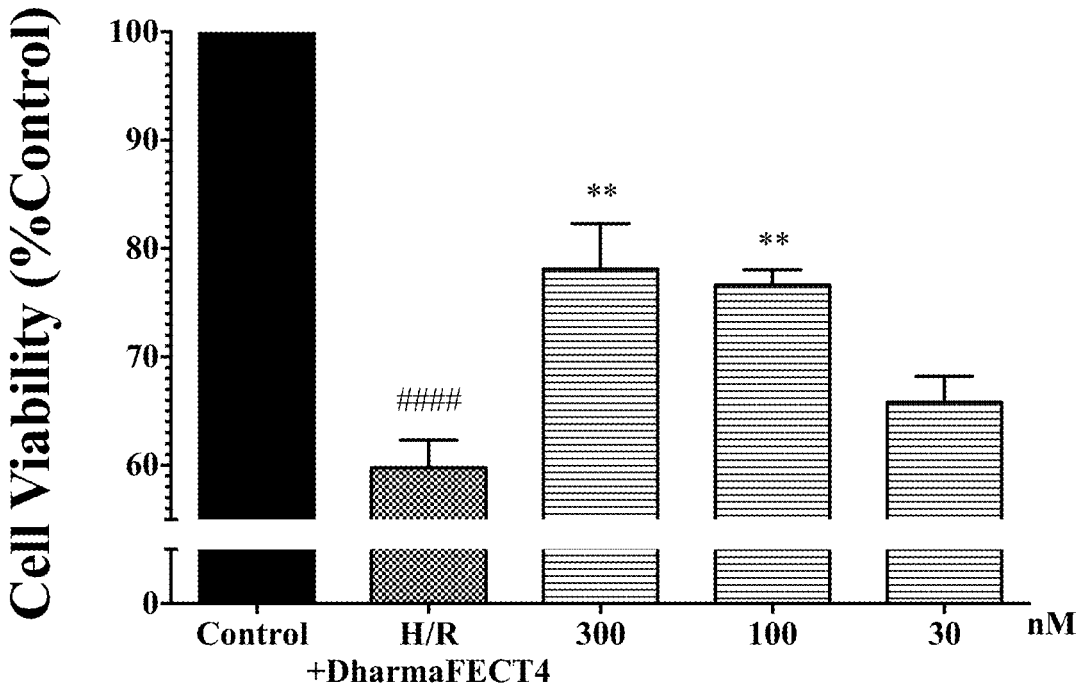

Fig.11A

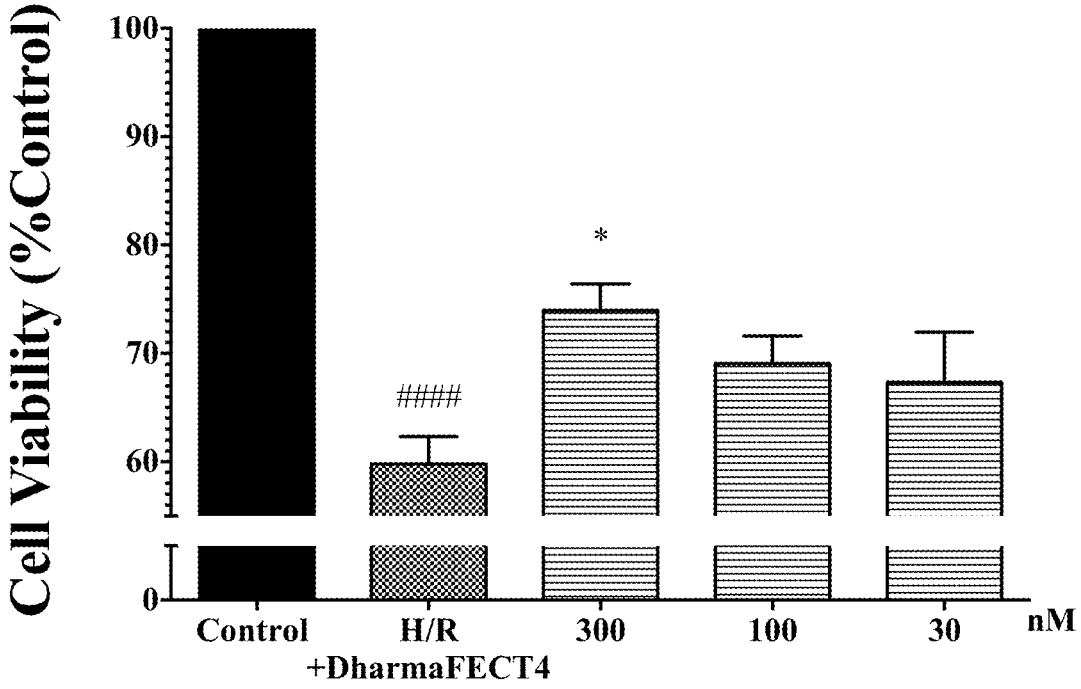

Fig.11B

METHODS AND COMPOSITIONS FOR PREVENTING OR TREATING HEART DISEASE

CROSS-REFERENCE TO RELATED APPLICATION

[0001] This application claims priority to, and the benefit of, Chinese Patent Application No. 20190784150.9 filed on Aug. 23, 2019. The entire contents of the foregoing application are hereby incorporated by reference for all purposes.

REFERENCE TO SEQUENCE LISTING

[0002] This application contains a sequence listing which has been submitted electronically in ASCII format and is hereby incorporated by reference in its entirety. Said ASCII copy, created on Oct. 13, 2020, is named "M006_091_NPRUS_Sequence_list_revised.txt" and is 104468 bytes in size.

TECHNICAL FIELD

[0003] The present invention belongs to the field of biomedicine, relating to a method of preventing or treating a subject suffering from heart disease comprising administration of transfer RNA molecules isolated from or derived from a plant of the genus *Panax* to the subject. The invention further relates to a pharmaceutical composition comprising a nucleic acid for the treatment and use thereof.

BACKGROUND OF THE INVENTION

[0004] Coronary heart disease (CHD) has become the top leading cause of mortality and morbidity worldwide. Traditional Chinese medicines (TCMs) have been widely applied for preventing or treating CHD whereas lots of research efforts have been contributed to investigate the effectiveness of isolated small molecules such as saponins, terpenoids, flavonoids or the like in treating CHD. Some ginsenosides have been found to have effect in protecting cardiomyocytes exposed to hypoxia/reoxygenation in vitro. However, most of them are often toxic to human. Also, macromolecules such as DNAs, RNAs, and proteins are generally considered unstable and have poor effect in living human body and therefore have not been widely considered as suitable in said treatment.

[0005] Currently, some studies show that non-coding RNAs (ncRNAs) such as microRNAs have diverse regulatory roles through targeting different aspects of RNA transcription or post-transcription process in nearly all eukaryotic organisms. Lin Zhang et al. (*Cell research* 2012, 22, 107-126) suggested that exogenous plant microRNAs in foods could be taken up by the mammalian gastrointestinal (GI) tract and entering into the circulation to various organs, where they are capable of regulating the expression of mammalian genes. Goodarzi, H. et al. (*Cell* 2015, 161 (4), 790-802) revealed that endogenous tRNA derived fragments could suppress the stability of multiple oncogenic transcripts in breast cancer cells through binding and antagonizing activities of pathogenesis-related RNA-binding proteins. Nevertheless, there still remains a need to derive effective molecules from various sources such as plants for treatments.

[0006] *Panax ginseng* C. A. Mey, a species from the family of Araliaceae, is considered to be the most precious herbs distributed mountainous regions of China and Korea. The roots of *P. ginseng* have been a famous traditional Chinese medicine used worldwide for thousands of years to be a tonic to invigorate weak bodies. In addition, the main component of *P. ginseng* such as ginsenosides and polysaccharides had been proved to show significant effects on cardioprotection. However, the dosage of these components is massive, which may cause toxicity to human bodies. Therefore, there remains a continuing need for new and improved treatments for patients with CHD and/or associated with different complications.

SUMMARY OF THE INVENTION

[0007] Therefore, in view of the inadequacy of existing technology, the purpose of the present invention is to provide transfer RNA molecules isolated from or derived from plant of genus *Panax* in the preparation of drugs for the prevention or treatment of heart diseases. Specifically, the purpose of the present invention is to identify or discover the key role of transfer RNA molecules isolated from or derived from plant of genus *Panax* in treatment of myocardial ischemia reperfusion, myocardial infarction, coronary heart disease, myocardial fibrosis and other cardiac diseases, and further application of diagnosis and treatment of these heart diseases.

[0008] The purpose of the invention is realized through the following technical scheme.

[0009] In a first aspect, the invention provides transfer RNA molecules and fragments derived from transfer RNA or its functional variants or homologous in the preparation of drugs for the prevention or treatment of a subject suffering from heart diseases, wherein said RNA molecule isolated from or derived from a plant of the genus *Panax*.

[0010] In an embodiment, the plant of the genus *Panax* comprises *Panax ginseng* C. A. Mey, *Panax notoginseng* (Burkill) F. H. Chen or *Panax quinquefolius* Linn. Preferably, said plant of the genus *Panax* is *Panax ginseng* C. A. Mey.

[0011] Preferably, the transfer RNA molecule comprises a sequence selected from SEQ ID NO: 465 to SEQ ID NO: 522.

[0012] In an alternative embodiment, the fragments derived from transfer RNA molecule is a double-stranded RNA molecule comprising a sense sequence selected from SEQ ID NO: 1 to SEQ ID NO: 232 or a functional variant or homologue therefore, and a complementary antisense sequence.

[0013] Preferably, the fragments derived from transfer RNA molecule is a double-stranded RNA molecule comprising a sense sequence selected from SEQ ID NO: 1 to SEQ ID NO: 40 or a functional variant or homologue therefore, and a complementary antisense sequence.

[0014] Wherein, said complementary antisense sequences of nucleotide sequences shown in any of SEQ ID NO:1 to SEQ ID NO:232 are showed in any of SEQ ID NO:233 to SEQ ID NO:464.

[0015] Preferably, the transfer RNA molecules and fragments derived from transfer RNA or its functional variants or homologous contains a 2 mer of 3' overhang.

[0016] Preferably, the transfer RNA molecules and fragments derived from transfer RNA or its functional variants or homologous contains a 3' cholesterol conjugation.

[0017] Preferably, the double-stranded RNA molecule comprises at least one modified nucleoside selected from inosine, 1-methyladenosine, 2-methyladenosine, N^6-meth-

yladenosine, N^6-isopentenyladenosine, 2'-O-methyladenosine, N^6-acetyladenosine, 1-methylinosine, pseudouridine, dihydrouridine, or 2-methylthio-N^6-methyladenosine.

[0018] In an embodiment, said heart diseases are selected from one or more of angina pectoris, myocardial infarction, myocardial ischemic injury, coronary heart disease, cardiac hypertrophy, and myocardial fibrosis.

[0019] In an embodiment, the RNA molecule of the invention is a non-coding molecule has a sequence length of from about 50 to 200 nucleotides or 10 to 30 base pairs.

[0020] In another aspect, the invention provides a pharmaceutical composition for preventing or treating heart diseases comprising an effective amount of transfer RNA molecule, fragments derived from transfer RNA molecules or its functional variants or homologous and a pharmaceutically tolerable vector, virus or excipient, wherein the RNA molecule is isolated or derived from a plant of the genus *Panax*.

[0021] In an embodiment, the pharmaceutically tolerable vector selected from one or more of the gene delivery vectors, chitosan, cholesterol, liposomes and nanoparticles.

[0022] Preferably, transfer RNA molecules, fragments derived from transfer RNA molecule or its functional variants or homologous are provided as composition containing a gene delivery vector.

[0023] Preferably, the pharmaceutical composition is provided by intravenous, intramuscular, intracoronary or direct myocardial injection.

[0024] In an embodiment, the pharmaceutical composition comprising the RNA molecule isolated or derived from the plant of the genus *Panax* comprises *Panax ginseng* C. A. Mey, *Panax notoginseng* (Burkill) F. H. Chen or *Panax quinquefolius* Linn. Preferably, said plant of the genus *Panax* is *Panax ginseng* C. A. Mey.

[0025] In an embodiment, wherein the transfer RNA molecule comprises a sequence selected from SEQ ID NO: 465 to SEQ ID NO: 522.

[0026] In an alternative embodiment, the fragments derived from transfer RNA molecule is a double-stranded RNA molecule comprising a sense sequence selected from SEQ ID NO: 1 to SEQ ID NO: 232 or a functional variant or homologue therefore, and a complementary antisense sequence.

[0027] Preferably, the fragments derived from transfer RNA molecule is a double-stranded RNA molecule comprising a sense sequence selected from SEQ ID NO: 1 to SEQ ID NO: 40 or a functional variant or homologue therefore, and a complementary antisense sequence.

[0028] Wherein, said complementary antisense sequences of nucleotide sequences shown in any of SEQ ID NO:1 to SEQ ID NO:232 are showed in any of SEQ ID NO:233 to SEQ ID NO:464.

[0029] Preferably, the transfer RNA molecules and fragments derived from transfer RNA or its functional variants or homologous comprises a 2 mer of 3' overhang.

[0030] Preferably, the transfer RNA molecules and fragments derived from transfer RNA or its functional variants or homologous comprises a 3' cholesterol conjugation.

[0031] Preferably, the transfer RNA molecules and fragments derived from transfer RNA or its functional variants or homologous comprises at least one modified nucleoside selected from inosine, 1-methyladenosine, 2-methyladenosine, N^6-methyladenosine, N^6-isopentenyladenosine, 2'-O-methyladenosine, N^6-acetyladenosine, 1-methylinosine, pseudouridine, dihydrouridine, or 2-methylthio-N^6-methyladenosine.

[0032] In an embodiment, said heart diseases are selected from one or more of angina pectoris, myocardial infarction, myocardial ischemic injury, coronary heart disease, cardiac hypertrophy, and myocardial fibrosis.

[0033] In an embodiment, the RNA molecule of the invention is a non-coding molecule has a sequence length of from about 50 to 200 nucleotides or 10 to 30 base pairs.

[0034] In a further aspect, the invention provides a method of preventing or treating a subject suffering from heart diseases, said method comprises the step of administering of an effective amount of transfer RNA molecules and fragments derived from transfer RNA or its functional variants or homologous thereof.

[0035] In an embodiment, said method comprising a step of contacting said cardiomyocytes with an effective amount of transfer RNA molecules and fragments derived from transfer RNA or its functional variants or homologous which are isolated or derived from a plant of the genus *Panax*.

[0036] In an embodiment, said plant of the genus *Panax* comprises *Panax ginseng* C. A. Mey, *Panax notoginseng* (Burkill) F. H. Chen or *Panax quinquefolius* Linn. Preferably, said plant of the genus *Panax* is *Panax ginseng* C. A. Mey.

[0037] Preferably, the transfer RNA molecule comprises a sequence selected from SEQ ID NO: 465 to SEQ ID NO: 522.

[0038] In an alternative embodiment, the fragments derived from transfer RNA molecule is a double-stranded RNA molecule comprising a sense sequence selected from SEQ ID NO: 1 to SEQ ID NO: 232 or a functional variant or homologue therefore, and a complementary antisense sequence.

[0039] Preferably, the fragments derived from transfer RNA molecule is a double-stranded RNA molecule comprising a sense sequence selected from SEQ ID NO: 1 to SEQ ID NO: 40 or a functional variant or homologue therefore, and a complementary antisense sequence.

[0040] Wherein, said complementary antisense sequences of nucleotide sequences shown in any of SEQ ID NO:1 to SEQ ID NO:232 are showed in any of SEQ ID NO:233 to SEQ ID NO:464.

[0041] Preferably, the transfer RNA molecules and fragments derived from transfer RNA or its functional variants or homologous contains a 2 mer of 3' overhang.

[0042] Preferably, the transfer RNA molecules and fragments derived from transfer RNA or its functional variants or homologous contains a 3' cholesterol conjugation.

[0043] Preferably, the double-stranded RNA molecule comprises at least one modified nucleoside selected from inosine, 1-methyladenosine, 2-methyladenosine, N^6-methyladenosine, N^6-isopentenyladenosine, 2'-O-methyladenosine, N^6-acetyladenosine, 1-methylinosine, pseudouridine, dihydrouridine, or 2-methylthio-N^6-methyladenosine.

[0044] In an embodiment, said heart diseases are selected from one or more of angina pectoris, myocardial infarction, myocardial ischemic injury, coronary heart disease, cardiac hypertrophy, and myocardial fibrosis.

[0045] In an embodiment, the RNA molecule of the invention is a non-coding molecule has a sequence length of from about 50 to 200 nucleotides or 10 to 30 base pairs.

[0046] Still further, the invention provides a recombinant vector comprising the double-stranded RNA molecule, wherein the double-stranded RNA molecule comprising a sense sequence selected from SEQ ID NO: 1 to SEQ ID NO: 232 or a functional variant or homologue therefore, and a complementary antisense sequence.

[0047] Preferably, the double-stranded RNA molecule comprising a sense sequence selected from SEQ ID NO: 1 to SEQ ID NO: 40 or a functional variant or homologue therefore, and a complementary antisense sequence.

[0048] Preferably, the double-stranded RNA molecule comprises a 2 mer of 3' overhang.

[0049] Preferably, the double-stranded RNA molecule comprises a 3' cholesterol conjugation.

[0050] Preferably, the double-stranded RNA molecule comprises at least one modified nucleoside selected from inosine, 1-methyladenosine, 2-methyladenosine, N^6-methyladenosine, N^6-isopentenyladenosine, 2'-O-methyladenosine, N^6-acetyladenosine, 1-methylinosine, pseudouridine, dihydrouridine, or 2-methylthio-N^6-methyladenosine.

[0051] Further, the invention provides the application in the preparation of drugs for the prevention or treatment of heart disease, wherein the drug comprises the transfer RNA molecule, fragments derived from transfer RNA molecule or its functional variant or homologous, the pharmaceutical composition and the recombinant vector.

[0052] The invention provides a novel and effective approach for treating heart diseases by administration of RNA molecules that are isolated or derived from a plant of the genus *Panax*, or in particular double-stranded RNA molecules comprising a sequence selected from SEQ ID NO: 1 to 232. Administration of said RNA molecules is also suitable for promoting the growth and proliferation of cardiomyocytes.

[0053] The inventors have found that non-coding RNA molecules isolated from a plant of the genus *Panax*, particularly transfer RNA molecules, and RNA molecules derived from *Panax* are particularly useful in treatment of heart diseases. The RNA molecules with a sequence length of about 10 to 200 nucleotides are highly effective at promoting the growth and proliferation of cardiomyocytes. Besides, said RNA molecules have restorative effects on the myocardial cytoskeleton after ischemia-reperfusion injury.

[0054] Those skilled in the art will appreciate that the invention described herein is susceptible to variations and modifications other than those specifically described. The invention includes all such variations and modifications. The invention also includes all steps and features referred to or indicated in the specification, individually or collectively, and any and all combinations of the steps or features.

[0055] Other features and aspects of the invention will become apparent by consideration of the following detailed description and accompanying figures.

BRIEF DESCRIPTION OF THE DRAWINGS

[0056] The patent or application file contains at least one drawing executed in color. Copies of this patent or patent application publication with color drawing(s) will be provided by the Office upon request and payment of the necessary fee.

[0057] The details about the implementation plan of the invention are elaborated in combination with the attached figures.

[0058] FIG. **1** shows gel electrophoresis profiles of RNA molecules from *Panax ginseng* C. A. Mey, including low range ssRNA Ladder (denoted as "L"), small RNA molecules (denoted as "S"), transfer RNAs (denoted as "T"), and individual transfer RNA including $tRNA^{Gly(GCC)}$, $tRNA^{His(GUG)}$, $tRNA^{Met(CAU)}$ (denoted as "Gly, His, Met" respectively), in accordance with an example embodiment.

[0059] FIG. **2** is a bar chart showing read length distribution of transfer RNAs from *Panax ginseng* C. A. Mey in accordance with an example embodiment.

[0060] FIG. **3**A is a bar chart showing the cardiomyocytes proliferation of 300 nM RNA molecules, $tRNA^{Gly(GCC)}$, $tRNA^{His(GUG)}$, $tRNA^{Met(CAU)}$ and $tRNA^{Leu(CAA)}$ from *Panax ginseng* C. A. Mey on H9C2 cell line exposed to hypoxia injury, compared to a control group, a hypoxia group in accordance with an example embodiment (mean±SD n=2; ****, p<0.0001 vs. vehicle hypoxia; ####, p<0.0001 vs. vehicle control).

[0061] FIG. **3**B is a bar chart showing the cardiomyocytes proliferation of 50 nM RNA molecules $tRNA^{Gly(GCC)}$, $tRNA^{His(GUG)}$, $tRNA^{Met(CAU)}$ and $tRNA^{Leu(CAA)}$ from *Panax ginseng* C. A. Mey on H9C2 cell line exposed to hypoxia/reoxygenation (H/R) injury, compared to a control group, a H/R group in accordance with an example embodiment (mean±SD n=3; *, p<0.05 vs. vehicle H/R; ####, p<0.0001 vs. vehicle control).

[0062] FIG. **4**A is a bar chart showing the cell viability of H9C2 cells after treatment with a RNA molecule $tRNA^{His(GUG)}$ at different concentrations, i.e. 100 nM, 50 nM, 25 nM, and 12.5 nM, compared to a control group, a H/R group in accordance with an example embodiment (mean±SD n=3; **, p<0.01, ***, p<0.001, ****, p<0.001 vs. vehicle H/R; ####, p<0.0001 vs. vehicle control).

[0063] FIG. **4**B is a bar chart showing the cell viability of H9C2 cells after treatment with a RNA molecule $tRNA^{Gly(GCC)}$ at different concentrations, i.e. 100 nM, 50 nM, 25 nM, and 12.5 nM, compared to a control group, a H/R group in accordance with an example embodiment (mean±SD n=3; *, p<0.05, **, p<0.01, ****, p<0.001 vs. vehicle H/R; ####, p<0.0001 vs. vehicle control).

[0064] FIG. **4**C is a bar chart showing the cell viability of H9C2 cells after treatment with Ginsenosides Rg1 at different concentrations, i.e. 100 μM, 25 μM, 6.25 μM, and 1.56 μM, compared to a control group, a H/R group in accordance with an example embodiment (mean±SD n=3; ****, p<0.0001 vs. vehicle H/R; ####, p<0.0001 vs. vehicle control).

[0065] FIG. **5**A is a bar chart showing the cell viability of H9C2 cells exposed to hypoxia/reoxygenation (H/R) injury after treatment with different RNA molecules derived from *Panax ginseng* C. A. Mey with a sequence length of 22 bp at a dose of 300 nM, compared to a control group, a H/R group in accordance with an example embodiment (mean±SD n=6; *, p<0.05 vs. vehicle H/R; ####, p<0.0001 vs. vehicle control).

[0066] FIG. **5**B is a bar chart showing the cell viability of H9C2 cells exposed to hypoxia/reoxygenation (H/R) injury after treatment with different RNA molecules derived from *Panax ginseng* C. A. Mey with a sequence length of 19 bp at a dose of 300 nM, compared to a control group, a H/R group in accordance with an example embodiment (mean±SD n=6; *, p<0.05 vs. vehicle H/R; ####, p<0.0001 vs. vehicle control).

[0067] FIG. **6**A is a bar chart showing the cell viability of H9C2 cells exposed to hypoxia/reoxygenation (H/R) injury

after treatment with RNA molecule HC50 at different concentrations, i.e. 900 nM, 300 nM, 30 nM, 3 nM and 0.3 nM, compared to a control group, a H/R group in accordance with an example embodiment (mean±SD n=3; *, p<0.05, ****, p<0.0001 vs. vehicle H/R; ####, p<0.0001 vs. vehicle control).

[0068] FIG. **6**B is a bar chart showing the cell viability of H9C2 cells exposed to hypoxia/reoxygenation (H/R) injury after treatment with RNA molecule HC83 at different concentrations, i.e. 900 nM, 300 nM, 30 nM, 3 nM and 0.3 nM, compared to a control group, a H/R group in accordance with an example embodiment (mean±SD n=3; **, p<0.01, ****, p<0.0001 vs. vehicle H/R; ####, p<0.0001 vs. vehicle control).

[0069] FIG. **7**A is a bar chart showing the mitochondrial viability of H9C2 cells exposed to hypoxia/reoxygenation (H/R) injury after treatment with RNA molecule HC50 at different concentrations, i.e. 300 nM, 100 nM, 30 nM, and 3 nM, compared to a control group, a H/R group in accordance with an example embodiment (mean±SD n=3; *, p<0.05 vs. vehicle H/R; ####, p<0.0001 vs. vehicle control).

[0070] FIG. **7**B is a bar chart showing the mitochondrial viability of H9C2 cells exposed to hypoxia/reoxygenation (H/R) injury after treatment with RNA molecule HC83 at different concentrations, i.e. 300 nM, 100 nM, 30 nM, and 3 nM, compared to a control group, a H/R group in accordance with an example embodiment (mean±SD n=3; ***, p<0.001, vs. vehicle H/R; ####, p<0.0001 vs. vehicle control).

[0071] FIG. **8**A is a cytoskeleton image showing protective effects on cytoskeleton destruction of H9C2 cells caused by hypoxia/reoxygenation (H/R) injury after treatment with RNA molecule HC50 at different concentrations, i.e. 900 nM, 300 nM, 100 nM, 30 nM, 10 nM, 3 nM, and 0.3 nM compared to a control group, a H/R group in accordance with an example embodiment.

[0072] FIG. **8**B is a cytoskeleton image showing protective effects on cytoskeleton destruction of H9C2 cells caused by hypoxia/reoxygenation (H/R) injury after treatment with RNA molecule HC83 at different concentrations, i.e. 900 nM, 300 nM, 100 nM, 30 nM, 10 nM, 3 nM, and 0.3 nM compared to a control group, a H/R group in accordance with an example embodiment.

[0073] FIG. **9**A is a bar chart showing the cell viability of H9C2 cells exposed to hypoxia/reoxygenation (H/R) injury after treatment with cholesterol-conjugated RNA molecule HC50 at different concentrations, i.e. 900 nM, 300 nM, 30 nM, 3 nM and 0.3 nM, compared to a control group, a H/R group in accordance with an example embodiment (mean±SD n=3; *, p<0.05, ****, p<0.0001 vs. vehicle H/R; ####, p<0.0001 vs. vehicle control).

[0074] FIG. **9**B is a bar chart showing the cell viability of H9C2 cells exposed to hypoxia/reoxygenation (H/R) injury after treatment with cholesterol-conjugated RNA molecule HC83 at different concentrations, i.e. 900 nM, 300 nM, 30 nM, 3 nM and 0.3 nM, compared to a control group, a H/R group in accordance with an example embodiment (mean±SD n=3; *, p<0.05, ***, p<0.001, ****, p<0.0001 vs. vehicle H/R; ####, p<0.0001 vs. vehicle control).

[0075] FIG. **10**A is a cytoskeleton image showing protective effects on cytoskeleton destruction of H9C2 cells caused by hypoxia/reoxygenation (H/R) injury after treatment with cholesterol-conjugated RNA molecule HC50 at different concentrations, i.e. 900 nM, 300 nM, 100 nM, 30 nM, 10 nM and 3 nM compared to a control group, a H/R group in accordance with an example embodiment.

[0076] FIG. **10**B is a cytoskeleton image showing protective effects on cytoskeleton destruction of H9C2 cells caused by hypoxia/reoxygenation (H/R) injury after treatment with cholesterol-conjugated RNA molecule HC83 at different concentrations, i.e. 900 nM, 300 nM, 100 nM, 30 nM, 10 nM and 3 nM compared to a control group, a H/R group in accordance with an example embodiment.

[0077] FIG. **11**A is a bar chart showing the cell viability of H9C2 cells exposed to hypoxia/reoxygenation (H/R) injury after treatment with RNA molecule HC50 at different concentrations, i.e. 300 nM, 100 nM and 30 nM, by transfected with DharmaFECT4 transfection reagent, compared to a control group, a H/R along with DharmaFECT4 treated group in accordance with an example embodiment (mean±SD n=3; **, p<0.01, vs. vehicle H/R+ DharmaFECT4; ####, p<0.0001 vs. vehicle control).

[0078] FIG. **11**B is a bar chart showing the cell viability of H9C2 cells exposed to hypoxia/reoxygenation (H/R) injury after treatment with RNA molecule HC83 at different concentrations, i.e. 300 nM, 100 nM and 30 nM, by transfected with DharmaFECT4 transfection reagent, compared to a control group, a H/R along with DharmaFECT4 treated group in accordance with an example embodiment (mean±SD n=3; *, p<0.05, vs. vehicle H/R+ DharmaFECT4; ####, p<0.0001 vs. vehicle control).

DETAILED DESCRIPTION OF THE EMBODIMENTS

[0079] Unless otherwise defined, all technical terms used herein have the same meaning as commonly understood by one skilled in the art to which the invention belongs.

[0080] As used herein, "comprising" means including the following elements but not excluding others. "Essentially consisting of" means that the material consists of the respective element along with usually and unavoidable impurities such as side products and components usually resulting from the respective preparation or method for obtaining the material such as traces of further components or solvents. "Consisting of" means that the material solely consists of, i.e. is formed by the respective element. As used herein, the forms "a," "an," and "the," are intended to include the singular and plural forms unless the context clearly indicates otherwise.

[0081] The present invention in the first aspect provides a method of preventing or treating a subject suffering from heart disease comprising administration of transfer RNA molecules and fragments derived from transfer RNA molecules or its functional variants or homologous to the subject, wherein the RNA molecules isolated from or derived from a plant of the genus *Panax*. The RNA molecule administered according to the present invention may be naturally present, modified or artificially synthesized according to the sequences disclosed in the present invention, and preferably the RNA molecule is isolated or derived from a plant of the genus *Panax*. The RNA molecule of the present invention is not provided in the form of boiled extract obtained from the plant such as decoction, as it would be appreciated that RNA molecule is susceptible to spontaneous degradation at elevated temperature, alkaline pH, and the presence of nucleases or divalent metal ions.

[0082] The RNA molecule of the present invention has a sequence length of from about 10 to 200 nucleotides which

can be regarded as a small RNA molecule. Preferably, the RNA molecule has a sequence length of from about 50 to about 200 nucleotides, from about 60 to about 150 nucleotides, in particular from about 70 to about 100 nucleotides.

[0083] The RNA molecule of the present invention comprises a sequence selected from SEQ ID NO: 1 to SEQ ID NO: 232 or a functional variant or homologue thereof. The term "functional variant" of the RNA molecule refers to a molecule substantially similar to said RNA molecule with one or more sequence alterations that do not affect the biological activity or function of the RNA molecule. The alterations in sequence that do not affect the functional properties of the resultant RNA molecules are well known in the art. For example, nucleotide changes which result in alteration of the -5'-terminal and -3'-terminal portions of the molecules would not be expected to alter the activity of the polynucleotides. In an embodiment, the RNA molecule of the present invention comprises at least one modified nucleoside selected from inosine, 1-methyladenosine, 2-methyladenosine, N^6-methyladenosine, N^6-isopentenyladenosine, 2'-O-methyladenosine, N^6-acetyladenosine, 1-methylinosine, pseudouridine, dihydrouridine, or 2-methylthio-N^6-methyladenosine.

[0084] In particular, the functional variant of the RNA molecule has at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% overall sequence identity to the non-variant RNA molecule according to the present invention.

[0085] The term "homologue" used herein refers to nucleotides having a sequence identity of at least 50%, at least 60%, at least 70%, at least 80%, at least 90% or at least 95% to the RNA molecules according to the present invention. In an embodiment, the homologue of the RNA molecule has at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% overall sequence identity to the RNA molecule.

[0086] In an embodiment, the RNA molecule is a non-coding molecule preferably selected from a transfer RNA molecule, a micro RNA molecule or a siRNA molecule; and more preferably is a transfer RNA molecule. tRNA molecules are highly conserved RNAs with function in various cellular processes such as reverse transcription, porphyrin biosynthesis or the like. In a particular embodiment, the RNA molecule of the invention comprises a sequence selected from SEQ ID NO: 465 to SEQ ID NO: 522 or a functional variant or homologue thereof; or the RNA molecule comprises SEQ ID NO: 465 to SEQ ID NO: 468 or a functional variant or homologue thereof; or the RNA molecule consists of a sequence selected from SEQ ID NO: 465 to SEQ ID NO: 522 or SEQ ID NO: 465 to SEQ ID NO: 468 or a functional variant or homologue thereof.

[0087] In an alternative embodiment where the RNA molecule is a small RNA molecule having a sequence length of from about 10 to about 30 base pairs, from about 15 to about 25 base pairs, from about 19 to about 22 base pairs, 19 base pairs or 22 base pairs. The RNA molecule comprises a sequence selected from SEQ ID NO: 1 to SEQ ID NO: 232 or a functional variant or homologue thereof, in particular SEQ ID NO: 1 to SEQ ID NO: 40 or a functional variant or homologue thereof; or consists of a sequence selected from SEQ ID NO: 1 to SEQ ID NO: 232, in particular SEQ ID NO: 1 to SEQ ID NO: 40 or a functional variant or homologue thereof.

[0088] Preferably, the RNA molecule is a double-stranded RNA molecule having a sense sequence selected from SEQ ID NO: 1 to SEQ ID NO: 232 or a functional variant or homologue thereof, and a complementary antisense sequence.

[0089] The antisense sequence is complementary to the sense sequence and therefore the antisense sequence is preferably selected from SEQ ID NO: 233 to 464 or functional variant or homologue thereof. In a particular embodiment, the double-stranded RNA molecule of the present invention has a sense sequence selected from SEQ ID NO: 1 to SEQ ID NO: 40 or a functional variant or homologue thereof, and a complementary antisense sequence selected from SEQ ID NO: 233 to SEQ ID NO: 272 or a functional variant or homologue thereof. The inventors unexpectedly found that the double-stranded RNA molecules of the present invention are particularly useful in treatment of heart diseases as described in detail below.

[0090] The RNA molecule of the present invention is preferably isolated or derived from the plant of the genus *Panax*. The plant of the genus *Panax* includes but is not limited to *Panax ginseng* C. A. Mey, *Panax quinquefolius* Linn., *Panax notoginseng* (Burkill) F. H. Chen, *Panax pseudoginseng* Wall, *Panax zingiberensis* C. Y. Wu et K. M. Feng. The plant of the genus *Panax* may be the source of Ginsenosides Rg1. In an embodiment, the RNA molecule is isolated or derived from *Panax ginseng* C. A. Mey.

[0091] In more detail, the RNA molecule of the present invention is preferably isolated or derived from the different plant organs of the genus *Panax*. The plant organs of the genus *Panax* includes but is not limited to leaves, roots, and fruits. In an embodiment, the RNA molecule is isolated or derived from the roots of *Panax ginseng* C. A. Mey.

[0092] In more detail, the preferred sequences of the RNA molecules of the present invention are listed in Tables 1 and 2 below. In an embodiment, RNA molecules of SEQ ID NO: 465 to SEQ ID NO: 522 as shown in Table 1 are isolated from a plant of genus *Panax* in particular from *Panax ginseng* C. A. Mey. These sequences are obtained by extraction, RNA isolation and purification of the plant. The inventors determined these RNA molecules are associated with chloroplasts, cytoplast and mitochondria. One possible approach to obtain the RNA molecules from a particular plant *Panax ginseng* C. A. Mey is illustrated in Example 1. It would be appreciated that other suitable methods for obtaining the isolated and purified RNA molecules of the present invention according to the disclosure herein can be applied, and the methods can be subject to appropriate modification to obtain an improved yield of the RNA molecules, without departing from the scope of the present invention.

TABLE 1

RNA molecules in particular tRNAs isolated from *Panax ginseng* C. A. Mey according to the present invention.

SEQ ID NO.	tRNA(s)	Sequence (5' to 3')	Length (mer)
465	$tRNA^{His\,(GUG)}$	GCGGAUGUAGCCAAGUGGAUCAAGGCAGUGGAUUGUGAA UCCACCAUGCGCGGGUUCAAUUCCCGUCGUUCGCCCCA	77
466	$tRNA^{Gly\,(GCC)}\_1$	GCGGAUAUAGUCGAAUGGUAAAAUUUCUCUUUGCCAAGGA GAAGACGCGGGUUCGAUUCCCGCUAUCCGCCCCA	74
467	$tRNA^{Leu\,(CAA)}$	GCCUUGGUGGUGAAAUGGUAGACACGCGAGACUCAAAAU CUCGUGCUAAAGAGCGUGGAGGUUCGAGUCCUCUUCAAG GCACCA	84
468	$tRNA^{Met\,(CAU)}\_1$	CGCGGAGUAGAGCAGUUUGGUAGCUCGCAAGGCUCAUAA CCUUGAGGUCACGGGUUCAAAUCCUGUCUCCGCAACCA	77
469	$tRNA^{Asp\,(GUC)}$	GGGAUUGUAGUUCAAUCGGUCAGAGCACCGCCCUGUCAA GGCGGAAGCUGCGGGUUCGAGCCCCGUCAGUCCCGCCA	77
470	$tRNA^{Ser\,(GCU)}\_1$	GGAGAGAUGGCUGAGUGGACUAAAGCGGCGGAUUGCUAA UCCGCUGUACGAGUUAUUCGUACCGAGGGUUCGAAUCCC UCUCUUUCCGCCA	91
471	$tRNA^{Gln\,(UUG)}\_1$	UGGGGCGUGGCCAAGUGGUAAGGCAACGGGUUUUGGUCC CGCUAUUCGGAGGUUCGAAUCCUUCCGUCCCAGCCA	75
472	$tRNA^{Glu\,(UUC)}\_1$	GCCCCCAUCGUCUAGUGGUUCAGGACAUCUCUCUUUCAA GGAGGCAGCGGGGAUUCGACUUCCCCUGGGGGUACCA	76
473	$tRNA^{Asn\,(GUU)}$	UCCUCAGUAGCUCAGUGGUAGAGCGGUCGGCUGUUAACU GACUGGUCGUAGGUUCGAAUCCUACCUGGGGAGCCA	75
474	$tRNA^{Pro\,(UGG)}\_1$	AGGGAUGUAGCGCAGCUUGGUAGCGCUUUUGUUUUGGGU ACAAAAUGUCACGGGUUCAAAUCCUGUCAUCCCUACCA	74
475	$tRNA^{Gln\,(CUG)}$	GGUUCCAUGGUCUAGUGGUCAGGACAUUGGACUCUGAAU CCAGUAACCCGAGUUCAGGUCUC GGUGGAACCUCCA	75
476	$tRNA^{Glu\,(UUG)}$	UCCGUUGUCGUCCAGCGGUUAGGAUAUCUGGCUUUCACC CAGGAGACCCGGGUUCGUUUCCCGGCAACGGAACCA	75
477	$tRNA^{Cys\,(GCA)}$	GGCUAGGUAACAUAAUGGAAAUGUAUUGGACUGCAAAUCC UGGAAUGACGGUUCGACCCCGUCCUUGGCCUCCA	74
478	$tRNA^{Met\,(CAU)}$	AGCGGGGUAGAGUAAUGGUCAACUCAUCAGUCUCAUUAU CUGAAGACUACAGGUUCGAAUCCUGUCCCCGCCUCCA	76
479	$tRNA^{Pro\,(UGG)}\_2$	CGAGGUGUAGCGCAGUCUGGUCAGCGCAUCUGUUUUGGG UACAGAGGGCCAUAGGUUCGAAUCCUGUCACCUUGACCA	78
480	$tRNA^{Gly\,(GCC)}\_2$	GCACCAGUGGUCUAGUGGUAGAAUAGUACCCUGCCACGG UACAGACCCGGGUUCGUUUCCCGGCUGGUGCACCA	74
481	$tRNA^{Asp\,(GUC)}$	GUCGUUGUAGUAUAGUGGUAAGUAUUCCCGCCUGUCACG CGGGUGACCCGGGUUCGAUCCCCGGCAACGGCGCCA	75
482	$tRNA^{Try\,(GCA)}$	CCGACCUUAGCUCAGUUGGUAGAGCGGAGGACUGUAGUG UGCUCGUAGCUAUCCUUAGGUCGCUGGUUCGAAUCCGGC UGGUCGGACCA	89
483	$tRNA^{Ala\,(AGC)}$	GGGGAUGUAGCUCAGAUGGUAGAGCGCUCGCUUAGCAUG CGAGAGGUACGGGGAUCGAUACCCCGCAUCUCCACCA	76
484	$tRNA^{Glu\,(CUC)}$	UCCGUUGUAGUCUAGUUGGUCAGGAUACUCGGCUCUCAC CCGAGAGACCCGGGUUCAAGUCCCGGCAACGGAACCA	76
485	$tRNA^{Glu\,(UUC)}\_2$	GUCCCUUUCGUCCAGUGGUUAGGACAUCGUCUUUUCAUG UCGAAGACACGGGUUCGAUUCCCGUAAGGGGUACCA	75
486	$tRNA^{Arg\,(CCU)}$	GCGCCUGUAGCUCAGUGGAUAGAGCGUCUGUUUCCUAAG CAGAAAGUCGUAGGUUCGACCCCUACCUGGCGCGCCA	76
487	$tRNA^{Val\,(AAC)}$	GGUUUCGUGGUGUAGUUGGUUAUCACGUCAGCCUAACAC ACUGAAGGUCUCCGGUUCGAACCCGGGCGAAGCCACCA	77

TABLE 1-continued

RNA molecules in particular tRNAs isolated from *Panax ginseng* C. A. Mey according to the present invention.

SEQ ID NO.	tRNA(s)	Sequence (5' to 3')	Length (mer)
488	$tRNA^{Val(CAC)}$	GUCUGGGUGGUGUAGUCGGUUAUCAUGCUAGUCUCACAC ACUAGAGGUCCCCGGUUCGAACCCGGGCUCAGACACCA	77
489	$tRNA^{Ser(UGA)}$	GGAUGGAUGUCUGAGCGGUUGGAAGAGUCGGUCUUGAAA ACCGAAGUAUUGAUAGGAAUACCGGGGGUUCGAAUCCCU CUCCAUCCGCCA	90
490	$tRNA^{Phe(GAA)}\_1$	GCGGGGAUAGCUCAGUUGGGAGAGUGUCAGACUGAAGAU CUAAAGGUCACGUGUUUGAUCCACGUUCACCGCACCA	76
491	$tRNA^{His(CAU)}$	GCAUCCAUGGCUGAAUGGUUAAAGCGCCCAACUCAUAAUU GGCGAAUUCGUAGGUUCAAUUCCUACUGGAUGCACCA	77
492	$tRNA^{Lys(UUU)}\_1$	GGGUUGCUAACUCAACGGUAGAGUACUCGGCUUUUAACC GACUAGUUCCGGGUUCGAAUCCCGGGCAACCCACCA	75
493	$tRNA^{Ser(UGA)}$	GGAGAGAUGGCUGAGUGGUUGAUAGCUCCGGUCUUGAAA ACCGGCAUAGUUUUAACAAAGAACUAUCGAGGGUUCGAAU CCCUCUCUCUCCUCCA	95
494	$tRNA^{Ser(GGA)}$	AGGAGAGAUGGCCGAGUGGUUGAAGGCGUAGCAUUGGAA CUGCUAUGUAGGCUUUUGUUUACCGAGGGUUCGAAUCCC UCUCUUUCCGCCA	91
495	$tRNA^{Gly(UCC)}$	GCGGGUAUAGUUUAGUGGUAAAACCCUAGCCUUCCAAGC UAACGAUGCGGGUUCGAUUCCCGCUACCCGCUCCA	74
496	$tRNA^{Arg(UCU)}$	GCGUCCAUUGUCUAAUGGAUAGGACAGAGGUCUUCUAAA CCUUUGGUAUAGGUUCAAAUCCUAUUGGACGCACCA	75
497	$tRNA^{Arg(ACG)}$	GGGCCUGUAGCUCAGAGGAUUAGAGCACGUGGCUACGAA CCACGGUGUCGGGGGUUCGAAUCCCUCCUCGCCCACCA	77
498	$tRNA^{Cys(GCA)}$	GGCGAUAUGGCCGAGUGGUAAGGCGGGGGACUGCAAAUC CUUUUUUCCCCAGUUCAAAUCCGGGUGUCGCCUCCA	75
499	$tRNA^{Tyr(GUA)}\_1$	GGGUCGAUGCCCGAGCGGUUAAUGGGGACGGACUGUAAA UUCGUUGGCAAUAUGUCUACGCUGGUUCAAAUCCAGCUC GGCCCACCA	87
500	$tRNA^{Thr(GGU)}$	GCCCUUUUAACUCAGCGGUAGAGUAACGCCAUGGUAAGG CGUAAGUCAUCGGUUCAAAUCCGAUAAGGGGCUCCA	75
501	$tRNAT^{hr(UGU)}$	GCCUGCUUAGCUCAGAGGUUAGAGCAUCGCAUUUGUAAU GCGAUGGUCAUCGGUUCGAUUCCGAUAGCCGGCUCCA	76
502	$tRNA^{Met(CAU)}\_2$	ACCUACUUAACUCAGUGGUUAGAGUAUUGCUUUCAUACGG CGGGAGUCAUUGGUUCAAAUCCAAUAGUAGGUACCA	76
503	$tRNA^{Leu(UAA)}$	GGGGAUAUGGCGGAAUUGGUAGACGCUACGGACUUAAAA UCCGUCGACUUUAAAAUCGUGAGGGUUCAAGUCCCUCUA UCCCCACCA	87
504	$tRNA^{Leu(UAG)}$	GCCGCUAUGGUGAAAUCGGUAGACACGCUGCUCUUAGGA AGCAGUGCUAGAGCAUCUCGGUUCGAGUCCGAGUGGCGG CACCA	83
505	$tRNA^{Phe(GAA)}\_2$	GUCGGGAUAGCUCAGCUGGUAGAGCAGAGGACUGAAAAU CCUCGUGUCACCAGUUCAAAUCUGGUUCCUGGCACCA	76
506	$tRN^{AVal(UAC)}$	AGGGCUAUAGCUCAGUUAGGUAGAGCACCUCGUUUACAC CGAGAAGGUCUACGGUCCGAGUCCGUAUAGCCCUACCA	77
507	$tRNA^{Val(GAC)}$	AGGGAUAUAACUCAGCGGUAGAGUGUCACCUUGACGUGG UGGAAGUCAUCAGUUCGAGCCUGAUUAUCCCUACCA	75
508	$tRNA^{Trp(CCA)}$	GCGCUCUUAGUUCAGUUCGGUAGAACGUGGGUCUCCAAA ACCCAAUGUCGUAGGUUCAAAUCCUACAGAGCGUGCCA	77

TABLE 1-continued

RNA molecules in particular tRNAs isolated from *Panax ginseng* C. A. Mey according to the present invention.

SEQ ID NO.	tRNA(s)	Sequence (5' to 3')	Length (mer)
509	$tRNA^{Ile\,(GAU)}$	GGGCUAUUAGCUCAGUGGUAGAGCGCGCCCCUGAUAAGG GCGAGGUCUCUGGUUCAAGUCCAGGAUGGCCCACCA	77
510	$tRNA^{Ala\,(UGC)}$	GGGGAUAUAGCUCAGUUGGUAGAGCUCCGCUCUUGCAAG GCGGAUGUCAGCGGUUCGAGUCCGCUUAUCUCCACCA	76
511	$tRNA^{Lys\,(UUU)}$_2	GGGUGUAUAGCUCAGUUGGUAGAGCAUUGGGCUUUUAAC CUAAUGGUCGCAGGUUCAAGUCCUGCUAUACCCACCA	76
512	$tRNA^{Lys\,(CUU)}$	CACCCUGUAGCUCAGAGGAAGAGUGGUCGUCUCUUAGCU GACAGGUCGUAGGUUCAAGUCCUACCAGGUUACCCA	75
513	$tRNA^{Gln\,(UUG)}$_2	UGGAGUAUAGCCAAGUGGUAAGGCACCGGUUUUUGGUAC CGAGGUUCGAAUCCUUUUACUCCAGCCA	67
514	$tRNA^{Met\,(CAU)}$_3	GGGCUUAUAGUUUAAUUGGUUGAAACGUACCGCUCAUAAC GGUUAUAUUGUAGGUUCGAGCCCUACUAAGCCUACCA	77
515	$tRNA^{Met\,(CAU)}$_4	GCAUCCAUGGCUGAAUGGUUAAAGCGCCCAACUCAUAAUU GGCGAAUUCGUAGGUUCAAUUCCUACUGGAUGCACCA	77
516	$tRNA^{Tyr\,(GUA)}$_2	GGGAGAGUGGCCGAGUGGUCAAAAGCGACAGACUGUAAA UCUGUUGAAGUUUUUCUACGUAGGUUCGAAUCCUGCCUC UCCCACCA	86
517	$tRNA^{Ser\,(GCU)}$_2	GGAGGUAUGGCUGAGUGGCUUAAGGCAUUGGUUUGCUAA AUCGACAUACAAGAAGAUUGUAUCAUGGGUUCGAAUCCCA UUUCCUCCGCCA	91
518	$tRNA^{Phe\,(GAA)}$_3	GUUCAGGUAGCUCAGCUGGUUAGAGCAAAGGACUGAAAA UCCUUGUGUCAGUGGUUCGAAUCCACUUCUAAGCGCCA	77
519	$tRNA^{Phe\,(AAA)}$	GUAACGAUCGAAUAAUGGAAGUUCACGGGGAAAGUCACUA GACCCGAAGCAUUGGUUCAAAUCCAAUUCGUUACUCCA	78
520	$tRNA^{Pro\,(UGG)}$_3	AGGGAUGUAGCGCAGCUUGGUAGCGCCUUUGUUUUGGGU AAAAAAUGUCACGGGUUCCAAUCCAAUCCUGUCAUCCCUA CCA	82
521	$tRNA^{Ile\,(CAU)}$	GGGCUAUUAGCUCAGUGGUAGAGCGCGCCCCUGAUAAGG GCGAGGUCUCUGGUUCAAGUCCAGGAUGGCCCACCA	75
522	$tRNA^{Gly\,(GCC)}$_3	GCGGAAAUAGCUUAAUGGUAGAGCAUAGCCUUGCCAAGG CUGAGGUUGAGGGUUCAAGUCCCUCCUUCCGCUCCA	75

[0093] The sense sequences of SEQ ID NO: 1 to SEQ ID NO: 232 and the antisense sequences of SEQ ID NO: 233 to SEQ ID NO: 464 as shown in Table 2 are artificially synthesized in accordance with the present invention. In particular, these sequences are derived sequence fragments prepared according to the sequences in Table 1 isolated from *Panax ginseng* C. A. Mey. The double-stranded RNA molecules are classified into 3 groups: the first group is 5'-terminal group (5'-t) containing a 5' terminal portion of the corresponding full-length mature tRNA molecules, forming segments of 2-35 nucleotides in length that are cut off in the D-ring, D-arm, anti-codon ring, or anti-codon ring arm. The second group is 3'-terminal group (3'-t) containing a 3' terminal portion with CCA tail of the corresponding full-length mature tRNA molecules, forming segments of 2-35 nucleotides in length that are cut off in the T-ring, T-arm, anti-codon ring, or anti-codon ring arm. The third group is anticodon group RNA molecules containing the anticodon loop portion of the corresponding full-length mature tRNA molecules, forming segments of 2-24 nucleotides in length that are cut off in anti-codon ring, or anti-codon ring arm. In the embodiment, tRFs derived from $tRNA^{His(GUG)}$ comprises 5'-tRFs "GCGGAUGUAGCCAAGUGGAUCA" that belongs to the family of 5'-tRFs with a length of 22 mer, 3'-tRFs "UCAAUUCCCGUCGUUCGCCCCA" that belongs to the family of 3'-tRFs with a length of 22 mer, 5'-tRFs "GCGGAUGUAGCCAAGUGGA" that belongs to the family of 5'-tRFs with a length of 19 mer, and 3'-tRFs "AUUCCCGUCGUUCGCCCCA" that belongs to the family of 3'-tRFs with a length of 19 mer, and anti-codon-tRFs "GUGGAUUGUGAAUCCAC" belongs to the family of anti-codon-tRFs with length of 17 mer.

[0094] Each of the sense sequences together with the corresponding antisense sequence form a double-stranded RNA molecule. As shown in Table 2, the sense sequence of SEQ ID NO: 1 and the antisense sequence of SEQ ID NO: 233 form a double-stranded RNA molecule with a length of 22 base pairs, and the resultant RNA molecule is denoted as HC70 for easy reference. Similarly, the sense sequence of SEQ ID NO: 2 and the antisense sequence of SEQ ID NO:

234 form a double-stranded RNA molecule with a length of 19 base pairs, and the resultant RNA molecule is denoted as HC50. Other RNA molecules of the present invention are presented in the Table 2.

[0095] The double-stranded RNA molecules are classified into 2 groups, namely a 5'-terminal group (5'-t), and a 3'-terminal group (3'-t). The 5'-t group RNA molecules contain a 5' terminal portion of the corresponding full-length RNA molecules isolated from the plant; and the 3'-t group RNA molecules contain a 3' terminal portion of the corresponding full-length RNA molecules isolated from the plant.

[0096] In another embodiment, RNA molecules may contain the anticodon loop portion of the corresponding full-length RNA molecules isolated from the plant and referred as anticodon group RNA molecules. The sense sequences of SEQ ID NO: 1 to SEQ ID NO: 232 can be generated by cleavage at different sites on the full-length RNA molecules SEQ ID NO: 465 to 522.

[0097] In addition, the RNA molecule of the present invention may comprise a 3' overhang, preferably comprise 2 mer of 3' overhangs. The provision of the 3' overhang improves the stability of the RNA molecules.

TABLE 2

RNA molecules derived from the sequences in Table 1 through artificial synthesis according to the present invention.

Source	Code	SEQ ID NO.	Sense sequence (5' to 3')	SEQ ID NO.	Antisense sequence (5' to 3')	Length (bp)	Group
$tRNA^{His(GUG)}$	HC70	1	GCGGAUGUAGCC AAGUGGAUCA	233	UGAUCCACUUGGC UACAUCCGC	22	5'-t
	HC50	2	GCGGAUGUAGCC AAGUGGA	234	UCCACUUGGCUAC AUCCGC	19	
	HC71	3	UCAAUUCCCGUC GUUCGCCCCA	235	UGGGGCGAACGA CGGGAAUUGA	22	3′-t
	HC51	4	AUUCCCGUCGUU CGCCCCA	236	UGGGGCGAACGA CGGGAAU	19	
$tRNA^{Asp(GUC)}$	HC72	5	GGGAUUGUAGUU CAAUCGGUCA	237	UGACCGAUUGAAC UACAAUCCC	22	5′-t
	HC52	6	GGGAUUGUAGUU CAAUCGG	238	CCGAUUGAACUAC AAUCCC	19	
	HC73	7	UCGAGCCCCGUC AGUCCCGCCA	239	UGGCGGGACUGA CGGGGCUCGA	22	3′-t
	HC53	8	AGCCCCGUCAGU CCCGCCA	240	UGGCGGGACUGA CGGGGCU	19	
$tRNA^{Gly(GCC)}$_1	HC74	9	GCGGAUAUAGUC GAAUGGUAAA	241	UUUACCAUUCGAC UAUAUCCGC	22	5′-t
	HC54	10	GCGGAUAUAGUC GAAUGGU	242	ACCAUUCGACUAU AUCCGC	19	
	HC75	11	UCGAUUCCCGCU AUCCGCCCCA	243	UGGGGCGGAUAG CGGGAAUCGA	22	3′-t
	HC55	12	AUUCCCGCUAUC CGCCCCA	244	UGGGGCGGAUAG CGGGAAU	19	
$tRNA^{Leu(CAA)}$	HC76	13	GCCUUGGUGGUG AAAUGGUAGA	245	UCUACCAUUUCAC CACCAAGGC	22	5′-t
	HC56	14	GCCUUGGUGGUG AAAUGGU	246	ACCAUUUCACCAC CAAGGC	19	
	HC77	15	UCGAGUCCUCUU CAAGGCACCA	247	UGGUGCCUUGAA GAGGACUCGA	22	3′-t
	HC57	16	AGUCCUCUUCAA GGCACCA	248	UGGUGCCUUGAA GAGGACU	19	
$tRNA^{Met(CAU)}$_1	HC78	17	CGCGGAGUAGAG CAGUUUGGUA	249	UACCAAACUGCUC UACUCCGCG	22	5′-t
	HC58	18	CGCGGAGUAGAG CAGUUUG	250	CAAACUGCUCUAC UCCGCG	19	
	HC79	19	UCAAAUCCUGUC UCCGCAACCA	251	UGGUUGCGGAGA CAGGAUUUGA	22	3′-t
	HC59	20	AAUCCUGUCUCC GCAACCA	252	UGGUUGCGGAGA CAGGAUU	19	
$tRNA^{Ser(GCU)}$_1	HC80	21	GGAGAGAUGGCU GAGUGGACUA	253	UAGUCCACUCAGC CAUCUCUCC	22	5′-t
	HC60	22	GGAGAGAUGGCU GAGUGGA	254	UCCACUCAGCCAU CUCUCC	19	
	HC81	23	GGAGAGAUGGCU GAGUGGACUA	255	UGGCGGAAAGAG AGGGAUUCGA	22	3′-t
	HC61	24	AAUCCCUCUCUU UCCGCCA	256	UGGCGGAAAGAG AGGGAUU	19	
$tRNA^{Gln(UUG)}$_1	HC82	25	UGGGGCGUGGC CAAGUGGUAAG	257	CUUACCACUUGG CCACGCCCCA	22	5′-t

TABLE 2-continued

RNA molecules derived from the sequences in Table 1 through artificial synthesis according to the present invention.

Source	Code	SEQ ID NO.	Sense sequence (5' to 3')	SEQ ID NO.	Antisense sequence (5' to 3')	Length (bp)	Group
	HC62	26	UGGGGCGUGGC CAAGUGGU	258	ACCACUUGGCCAC GCCCCA	19	
	HC83	27	UCGAAUCCUUCC GUCCCAGCCA	259	UGGCUGGGACGG AAGGAUUCGA	22	3′-t
	HC63	28	AAUCCUUCCGUC CCAGCCA	260	UGGCUGGGACGG AAGGAUU	19	
$tRNA^{Glu(UUC)}$_1	HC84	29	GCCCCCAUCGUC UAGUGGUUCA	261	UGAACCACUAGAC GAUGGGGGC	22	5′-t
	HC64	30	GCCCCCAUCGUC UAGUGGU	262	ACCACUAGACGAU GGGGGC	19	
	HC85	31	UCGACUUCCCCU GGGGGUACCA	263	UGGUACCCCCAG GGGAAGUCGA	22	3′-t
	HC65	32	ACUUCCCCUGGG GGUACCA	264	UGGUACCCCCAG GGGAAGU	19	
$tRNA^{Asn(GUU)}$	HC86	33	UCCUCAGUAGCU CAGUGGUAGA	265	UCUACCACUGAGC UACUGAGGA	22	5′-t
	HC66	34	UCCUCAGUAGCU CAGUGGU	266	ACCACUGAGCUAC UGAGGA	19	
	HC87	35	UCGAAUCCUACC UGGGGAGCCA	267	UGGCUCCCCAGG UAGGAUUCGA	22	3′-t
	HC67	36	AAUCCUACCUGG GGAGCCA	268	UGGCUCCCCAGG UAGGAUU	19	
$tRNA^{Pro(UGG)}$_1	HC88	37	AGGGAUGUAGCG CAGCUUGGUA	269	UACCAAGCUGCG CUACAUCCCU	22	5′-t
	HC68	38	AGGGAUGUAGCG CAGCUUG	270	CAAGCUGCGCUA CAUCCCU	19	
	HC89	39	GGUUCAAAUCCU GUCAUCCCUA	271	UAGGGAUGACAG GAUUUGAACC	22	3′-t
	HC69	40	UCAAAUCCUGUC AUCCCUA	272	UAGGGAUGACAG GAUUUGA	19	
$tRNA^{Gln(CUG)}$	HC90	41	GGUUCCAUGGUC UAGUGGUCAG	273	CUGACCACUAGAC CAUGGAACC	22	5′-t
	HC91	42	GGUUCCAUGGUC UAGUGGU	274	ACCACUAGACCAU GGAACC	19	
	HC92	43	UCAGGUCUCGGU GGAACCUCCA	275	UGGAGGUUCCAC CGAGACCUGA	22	3′-t
	HC93	44	GGUCUCGGUGGA ACCUCCA	276	UGGAGGUUCCAC CGAGACC	19	
$tRNA^{Glu(UUG)}$	HC94	45	UCCGUUGUCGUC CAGCGGUUAG	277	CUAACCGCUGGA CGACAACGGA	22	5′-t
	HC95	46	UCCGUUGUCGUC CAGCGGU	278	ACCGCUGGACGA CAACGGA	19	
	HC96	47	UCGUUUCCCGGC AACGGAACCA	279	UGGUUCCGUUGC CGGGAAACGA	22	3′-t
	HC97	48	UUUCCCGGCAAC GGAACCA	280	UGGUUCCGUUGC CGGGAAA	19	
$tRNA^{Cys(GCA)}$	HC98	49	GGCUAGGUAACA UAAUGGAAAU	281	AUUUCCAUUAUGU UACCUAGCC	22	5′-t
	HC99	50	GGCUAGGUAACA UAAUGGA	282	UCCAUUAUGUUAC CUAGCC	19	
	HC100	51	UCGACCCCGUCC UUGGCCUCCA	283	UGGAGGCCAAGG ACGGGGUCGA	22	3′-t
	HC101	52	ACCCCGUCCUUG GCCUCCA	284	UGGAGGCCAAGG ACGGGGU	19	
$tRNA^{Met(CAU)}$_1	HC102	53	AGCGGGGUAGAG UAAUGGUCAA	285	UUGACCAUUACUC UACCCCGCU	22	5′-t
	HC103	54	AGCGGGGUAGAG UAAUGGU	286	ACCAUUACUCUAC CCCGCU	19	
	HC104	55	UCGAAUCCUGUC CCCGCCUCCA	287	UGGAGGCGGGGA CAGGAUUCGA	22	3′-t
	HC105	56	AAUCCUGUCCCC GCCUCCA	288	UGGAGGCGGGGA CAGGAUU	19	

TABLE 2-continued

RNA molecules derived from the sequences in Table 1 through artificial synthesis according to the present invention.

Source	Code	SEQ ID NO.	Sense sequence (5' to 3')	SEQ ID NO.	Antisense sequence (5' to 3')	Length (bp)	Group
$tRNA^{Pro(UGG)}$_2	HC106	57	CGAGGUGUAGCG CAGUCUGGUC	289	GACCAGACUGCG CUACACCUCG	22	5′-t
	HC107	58	CGAGGUGUAGCG CAGUCUG	290	CAGACUGCGCUA CACCUCG	19	
	HC108	59	UCGAAUCCUGUC ACCUUGACCA	291	UGGUCAAGGUGA CAGGAUUCGA	22	3′-t
	HC109	60	AAUCCUGUCACC UUGACCA	292	UGGUCAAGGUGA CAGGAUU	19	
$tRNA^{Gly(GCC)}$_2	HC110	61	GCACCAGUGGUC UAGUGGUAGA	293	UCUACCACUAGAC CACUGGUGC	22	5′-t
	HC111	62	GCACCAGUGGUC UAGUGGU	294	ACCACUAGACCAC UGGUGC	19	
	HC112	63	UCGUUUCCCGGC UGGUGCACCA	295	UGGUGCACCAGC CGGGAAACGA	22	3′-t
	HC113	64	UUUCCCGGCUGG UGCACCA	296	UGGUGCACCAGC CGGGAAA	19	
$tRNA^{Asp(GUC)}$	HC114	65	GUCGUUGUAGUA UAGUGGUAAG	297	CUUACCACUAUAC UACAACGAC	22	5′-t
	HC115	66	GUCGUUGUAGUA UAGUGGU	298	ACCACUAUACUAC AACGAC	19	
	HC116	67	UCGAUCCCCGGC AACGGCGCCA	299	UGGCGCCGUUGC CGGGGAUCGA	22	3′-t
	HC117	68	AUCCCCGGCAAC GGCGCCA	300	UGGCGCCGUUGC CGGGGAU	19	
$tRNA^{Try(GCA)}$	HC118	69	CCGACCUUAGCU CAGUUGGUAG	301	CUACCAACUGAGC UAAGGUCGG	22	5′-t
	HC119	70	CCGACCUUAGCU CAGUUGG	302	CCAACUGAGCUAA GGUCGG	19	
	HC120	71	UCGAAUCCGGCU GGUCGGACCA	303	UGGUCCGACCAG CCGGAUUCGA	22	3′-t
	HC121	72	AAUCCGGCUGGU CGGACCA	304	UGGUCCGACCAG CCGGAUU	19	
$tRNA^{Ala(AGC)}$	HC122	73	GGGGAUGUAGCU CAGAUGGUAG	305	CUACCAUCUGAGC UACAUCCCC	22	5′-t
	HC123	74	GGGGAUGUAGCU CAGAUGG	306	CCAUCUGAGCUAC AUCCCC	19	
	HC124	75	UCGAUACCCCGC AUCUCCACCA	307	UGGUGGAGAUGC GGGGUAUCGA	22	3′-t
	HC125	76	AUACCCCGCAUC UCCACCA	308	UGGUGGAGAUGC GGGGUAU	19	
$tRNA^{Glu(CUC)}$	HC126	77	UCCGUUGUAGUC UAGUUGGUCA	309	UGACCAACUAGAC UACAACGGA	22	5′-t
	HC127	78	UCCGUUGUAGUC UAGUUGG	310	CCAACUAGACUAC AACGGA	19	
	HC128	79	UCAAGUCCCGGC AACGGAACCA	311	UGGUUCCGUUGC CGGGACUUGA	22	3′-t
	HC129	80	AGUCCCGGCAAC GGAACCA	312	UGGUUCCGUUGC CGGGACU	19	
$tRNA^{Glu(UUC)}$_2	HC130	81	GUCCCUUUCGUC CAGUGGUUAG	313	CUAACCACUGGAC GAAAGGGAC	22	5′-t
	HC131	82	GUCCCUUUCGUC CAGUGGU	314	ACCACUGGACGAA AGGGAC	19	
	HC132	83	UCGAUUCCCGUA AGGGGUACCA	315	UGGUACCCCUUA CGGGAAUCGA	22	3′-t
	HC133	84	AUUCCCGUAAGG GGUACCA	316	UGGUACCCCUUA CGGGAAU	19	
$tRNA^{Arg(CCU)}$	HC134	85	GCGCCUGUAGCU CAGUGGAUAG	317	CUAUCCACUGAGC UACAGGCGC	22	5′-t
	HC135	86	GCGCCUGUAGCU CAGUGGA	318	UCCACUGAGCUAC AGGCGC	19	
	HC136	87	UCGACCCCUACC UGGCGCGCCA	319	UGGCGCGCCAGG UAGGGGUCGA	22	3′-t

TABLE 2-continued

RNA molecules derived from the sequences in Table 1 through artificial synthesis according to the present invention.

Source	Code	SEQ ID NO.	Sense sequence (5' to 3')	SEQ ID NO.	Antisense sequence (5' to 3')	Length (bp)	Group
	HC137	88	ACCCCUACCUGG CGCGCCA	320	UGGCGCGCCAGG UAGGGGU	19	
$tRNA^{Val\ (AAC)}$	HC138	89	GGUUUCGUGGUG UAGUUGGUUA	321	UAACCAACUACAC CACGAAACC	22	5′-t
	HC139	90	GGUUUCGUGGUG UAGUUGG	322	CCAACUACACCAC GAAACC	19	
	HC140	91	UCGAACCCGGGC GAAGCCACCA	323	UGGUGGCUUCGC CCGGGUUCGA	22	3′-t
	HC141	92	AACCCGGGCGAA GCCACCA	324	UGGUGGCUUCGC CCGGGUU	19	
$tRNA^{Val\ (CAC)}$	HC142	93	GUCUGGGUGGU GUAGUCGGUUA	325	UAACCGACUACAC CACCCAGAC	22	5′-t
	HC143	94	GUCUGGGUGGU GUAGUCGG	326	CCGACUACACCAC CCAGAC	19	
	HC144	95	UCGAACCCGGGC UCAGACACCA	327	UGGUGUCUGAGC CCGGGUUCGA	22	3′-t
	HC145	96	AACCCGGGCUCA GACACCA	328	UGGUGUCUGAGC CCGGGUU	19	
$tRNA^{Ser\ (UGA)}$	HC146	97	GGAUGGAUGUCU GAGCGGUUGG	329	CCAACCGCUCAGA CAUCCAUCC	22	5′-t
	HC147	98	GGAUGGAUGUCU GAGCGGU	330	ACCGCUCAGACAU CCAUCC	19	
	HC148	99	UCGAAUCCCUCU CCAUCCGCCA	331	UGGCGGAUGGAG AGGGAUUCGA	22	3′-t
	HC149	100	AAUCCCUCUCCA UCCGCCA	332	UGGCGGAUGGAG AGGGAUU	19	
$tRNA^{Phe\ (GAA)}$	HC150	101	GCGGGGAUAGCU CAGUUGGGAG	333	CUCCCAACUGAGC UAUCCCCGC	22	5′-t
	HC151	102	GCGGGGAUAGCU CAGUUGG	334	CCAACUGAGCUAU CCCCGC	19	
	HC152	103	UUGAUCCACGUU CACCGCACCA	335	UGGUGCGGUGAA CGUGGAUCAA	22	3′-t
	HC153	104	AUCCACGUUCAC CGCACCA	336	UGGUGCGGUGAA CGUGGAU	19	
$tRNA^{His\ (CAU)}$	HC154	105	GCAUCCAUGGCU GAAUGGUUAA	337	UUAACCAUUCAGC CAUGGAUGC	22	5′-t
	HC155	106	GCAUCCAUGGCU GAAUGGU	338	ACCAUUCAGCCAU GGAUGC	19	
	HC156	107	UCAAUUCCUACU GGAUGCACCA	339	UGGUGCAUCCAG UAGGAAUUGA	22	3′-t
	HC157	108	AUUCCUACUGGA UGCACCA	340	UGGUGCAUCCAG UAGGAAU	19	
$tRNA^{Lys\ (UUU)}$_1	HC158	109	GGGUUGCUAACU CAACGGUAGA	341	UCUACCGUUGAG UUAGCAACCC	22	5′-t
	HC159	110	GGGUUGCUAACU CAACGGU	342	ACCGUUGAGUUA GCAACCC	19	
	HC160	111	UCGAAUCCCGGG CAACCCACCA	343	UGGUGGGUUGCC CGGGAUUCGA	22	3′-t
	HC161	112	AAUCCCGGGCAA CCCACCA	344	UGGUGGGUUGCC CGGGAUU	19	
$tRNA^{Ser\ (UGA)}$	HC162	113	GGAGAGAUGGCU GAGUGGUUGA	345	UCAACCACUCAGC CAUCUCUCC	22	5′-t
	HC163	114	GGAGAGAUGGCU GAGUGGU	346	ACCACUCAGCCAU CUCUCC	19	
	HC164	115	UCGAAUCCCUCU CUCUCCUCCA	347	UGGAGGAGAGAG AGGGAUUCGA	22	3′-t
	HC165	116	AAUCCCUCUCUC UCCUCCA	348	UGGAGGAGAGAG AGGGAUU	19	
$tRNA^{Ser\ (GGA)}$	HC166	117	AGGAGAGAUGGC CGAGUGGUUG	349	CAACCACUCGGCC AUCUCUCCU	22	5′-t
	HC167	118	AGGAGAGAUGGC CGAGUGG	350	CCACUCGGCCAU CUCUCCU	19	

TABLE 2-continued

RNA molecules derived from the sequences in Table 1 through artificial synthesis according to the present invention.

Source	Code	SEQ ID NO.	Sense sequence (5' to 3')	SEQ ID NO.	Antisense sequence (5' to 3')	Length (bp)	Group
	HC168	119	UCGAAUCCCUCU CUUUCCGCCA	351	UGGCGGAAAGAG AGGGAUUCGA	22	3′-t
	HC169	120	AAUCCCUCUCUU UCCGCCA	352	UGGCGGAAAGAG AGGGAUU	19	
tRNA$^{Gly\,(UCC)}$	HC170	121	GCGGGUAUAGUU UAGUGGUAAA	353	UUUACCACUAAAC UAUACCCGC	22	5′-t
	HC171	122	GCGGGUAUAGUU UAGUGGU	354	ACCACUAAACUAU ACCCGC	19	
	HC172	123	UCGAUUCCCGCU ACCCGCUCCA	355	UGGAGCGGGUAG CGGGAAUCGA	22	3′-t
	HC173	124	AUUCCCGCUACC CGCUCCA	356	UGGAGCGGGUAG CGGGAAU	19	
tRNA$^{Arg\,(UCU)}$	HC174	125	GCGUCCAUUGUC UAAUGGAUAG	357	CUAUCCAUUAGAC AAUGGACGC	22	5′-t
	HC175	126	GCGUCCAUUGUC UAAUGGA	358	UCCAUUAGACAAU GGACGC	19	
	HC176	127	UCAAAUCCUAUU GGACGCACCA	359	UGGUGCGUCCAA UAGGAUUUGA	22	3′-t
	HC177	128	AAUCCUAUUGGA CGCACCA	360	UGGUGCGUCCAA UAGGAUU	19	
tRNA$^{Arg\,(ACG)}$	HC178	129	GGGCCUGUAGCU CAGAGGAUUA	361	UAAUCCUCUGAGC UACAGGCCC	22	5′-t
	HC179	130	GGGCCUGUAGCU CAGAGGA	362	UCCUCUGAGCUA CAGGCCC	19	
	HC180	131	UCGAAUCCCUCC UCGCCCACCA	363	UGGUGGGCGAGG AGGGAUUCGA	22	3′-t
	HC181	132	AAUCCCUCCUCG CCCACCA	364	UGGUGGGCGAGG AGGGAUU	19	
tRNA$^{Cys\,(GCA)}$	HC182	133	GGCGAUAUGGCC GAGUGGUAAG	365	CUUACCACUCGG CCAUAUCGCC	22	5′-t
	HC183	134	GGCGAUAUGGCC GAGUGGU	366	ACCACUCGGCCAU AUCGCC	19	
	HC184	135	UCAAAUCCGGGU GUCGCCUCCA	367	UGGAGGCGACAC CCGGAUUUGA	22	3′-t
	HC185	136	AAUCCGGGUGUC GCCUCCA	368	UGGAGGCGACAC CCGGAUU	19	
tRNA$^{Tyr\,(GUA)}$_1	HC186	137	GGGUCGAUGCCC GAGCGGUUAA	369	UUAACCGCUCGG GCAUCGACCC	22	5′-t
	HC187	138	GGGUCGAUGCCC GAGCGGU	370	ACCGCUCGGGCA UCGACCC	19	
	HC188	139	UCAAAUCCAGCU CGGCCCACCA	371	UGGUGGGCCGAG CUGGAUUUGA	22	3′-t
	HC189	140	AAUCCAGCUCGG CCCACCA	372	UGGUGGGCCGAG CUGGAUU	19	
tRNA$^{Thr\,(GGU)}$	HC190	141	GCCCUUUUAACU CAGCGGUAGA	373	UCUACCGCUGAG UUAAAAGGGC	22	5′-t
	HC191	142	GCCCUUUUAACU CAGCGGU	374	ACCGCUGAGUUAA AAGGGC	19	
	HC192	143	UCAAAUCCGAUA AGGGGCUCCA	375	UGGAGCCCCUUA UCGGAUUUGA	22	3′-t
	HC193	144	AAUCCGAUAAGG GGCUCCA	376	UGGAGCCCCUUA UCGGAUU	19	
tRNA$^{Thr\,(UGU)}$	HC194	145	GCCUGCUUAGCU CAGAGGUUAG	377	CUAACCUCUGAGC UAAGCAGGC	22	5′-t
	HC195	146	GCCUGCUUAGCU CAGAGGU	378	ACCUCUGAGCUAA GCAGGC	19	
	HC196	147	UCGAUUCCGAUA GCCGGCUCCA	379	UGGAGCCGGCUA UCGGAAUCGA	22	3′-t
	HC197	148	AUUCCGAUAGCC GGCUCCA	380	UGGAGCCGGCUA UCGGAAU	19	
tRNA$^{Met\,(CAU)}$_2	HC198	149	ACCUACUUAACU CAGUGGUUAG	381	CUAACCACUGAGU UAAGUAGGU	22	5′-t

TABLE 2-continued

RNA molecules derived from the sequences in Table 1 through artificial synthesis according to the present invention.

Source	Code	SEQ ID NO.	Sense sequence (5' to 3')	SEQ ID NO.	Antisense sequence (5' to 3')	Length (bp)	Group
	HC199	150	ACCUACUUAACU CAGUGGU	382	ACCACUGAGUUAA GUAGGU	19	
	HC200	151	UCAAAUCCAAUA GUAGGUACCA	383	UGGUACCUACUAU UGGAUUUGA	22	3′-t
	HC201	152	AAUCCAAUAGUA GGUACCA	384	UGGUACCUACUAU UGGAUU	19	
$tRNA^{Leu(UAA)}$	HC202	153	GGGGAUAUGGCG GAAUUGGUAG	385	CUACCAAUUCCGC CAUAUCCCC	22	5′-t
	HC203	154	GGGGAUAUGGCG GAAUUGG	386	CCAAUUCCGCCAU AUCCCC	19	
	HC204	155	UCAAGUCCCUCU AUCCCCACCA	387	UGGUGGGGAUAG AGGGACUUGA	22	3′-t
	HC205	156	AGUCCCUCUAUC CCCACCA	388	UGGUGGGGAUAG AGGGACU	19	
$tRNA^{Leu(UAG)}$	HC206	157	GCCGCUAUGGUG AAAUCGGUAG	389	CUACCGAUUUCAC CAUAGCGGC	22	5′-t
	HC207	158	GCCGCUAUGGUG AAAUCGG	390	CCGAUUUCACCAU AGCGGC	19	
	HC208	159	UCGAGUCCGAGU GGCGGCACCA	391	UGGUGCCGCCAC UCGGACUCGA	22	3′-t
	HC209	160	AGUCCGAGUGGC GGCACCA	392	UGGUGCCGCCAC UCGGACU	19	
$tRNA^{Phe(GAA)}$_2	HC210	161	GUCGGGAUAGCU CAGCUGGUAG	393	CUACCAGCUGAG CUAUCCCGAC	22	5′-t
	HC211	162	GUCGGGAUAGCU CAGCUGG	394	CCAGCUGAGCUA UCCCGAC	19	
	HC212	163	UCAAAUCUGGUU CCUGGCACCA	395	UGGUGCCAGGAA CCAGAUUUGA	22	3′-t
	HC213	164	AAUCUGGUUCCU GGCACCA	396	UGGUGCCAGGAA CCAGAUU	19	
$tRNA^{Val(UAC)}$	HC214	165	AGGGCUAUAGCU CAGUUAGGUA	397	UACCUAACUGAGC UAUAGCCCU	22	5′-t
	HC215	166	AGGGCUAUAGCU CAGUUAG	398	CUAACUGAGCUAU AGCCCU	19	
	HC216	167	CCGAGUCCGUAU AGCCCUACCA	399	UGGUAGGGCUAU ACGGACUCGG	22	3′-t
	HC217	168	AGUCCGUAUAGC CCUACCA	400	UGGUAGGGCUAU ACGGACU	19	
$tRNA^{Val(GAC)}$	HC218	169	AGGGAUAUAACU CAGCGGUAGA	401	UCUACCGCUGAG UUAUAUCCCU	22	5′-t
	HC219	170	AGGGAUAUAACU CAGCGGU	402	ACCGCUGAGUUA UAUCCCU	19	
	HC220	171	UCGAGCCUGAUU AUCCCUACCA	403	UGGUAGGGAUAA UCAGGCUCGA	22	3′-t
	HC221	172	AGCCUGAUUAUC CCUACCA	404	UGGUAGGGAUAA UCAGGCU	19	
$tRNA^{Trp(CCA)}$	HC222	173	GCGCUCUUAGUU CAGUUCGGUA	405	UACCGAACUGAAC UAAGAGCGC	22	5′-t
	HC223	174	GCGCUCUUAGUU CAGUUCG	406	CGAACUGAACUAA GAGCGC	19	
	HC224	175	UCAAAUCCUACA GAGCGUGCCA	407	UGGCACGCUCUG UAGGAUUUGA	22	3′-t
	HC225	176	AAUCCUACAGAG CGUGCCA	408	UGGCACGCUCUG UAGGAUU	19	
$tRNA^{Ile(GAU)}$	HC226	177	GGGCUAUUAGCU CAGUGGUAGA	409	UCUACCACUGAGC UAAUAGCCC	22	5′-t
	HC227	178	GGGCUAUUAGCU CAGUGGU	410	ACCACUGAGCUAA UAGCCC	19	
	HC228	179	UCAAGUCCAGGA UGGCCCACCA	411	UGGUGGGCCAUC CUGGACUUGA	22	3′-t
	HC229	180	AGUCCAGGAUGG CCCACCA	412	UGGUGGGCCAUC CUGGACU	19	

TABLE 2-continued

RNA molecules derived from the sequences in Table 1 through artificial synthesis according to the present invention.

Source	Code	SEQ ID NO.	Sense sequence (5' to 3')	SEQ ID NO.	Antisense sequence (5' to 3')	Length (bp)	Group
$tRNA^{Ala\ (UGC)}$	HC230	181	GGGGAUAUAGCU CAGUUGGUAG	413	CUACCAACUGAGC UAUAUCCCC	22	5′-t
	HC231	182	GGGGAUAUAGCU CAGUUGG	414	CCAACUGAGCUAU AUCCCC	19	
	HC232	183	UCGAGUCCGCUU AUCUCCACCA	415	UGGUGGAGAUAA GCGGACUCGA	22	3′-t
	HC233	184	AGUCCGCUUAUC UCCACCA	416	UGGUGGAGAUAA GCGGACU	19	
$tRNA^{Lys\ (UUU)}\_2$	HC234	185	GGGUGUAUAGCU CAGUUGGUAG	417	CUACCAACUGAGC UAUACACCC	22	5′-t
	HC235	186	GGGUGUAUAGCU CAGUUGG	418	CCAACUGAGCUAU ACACCC	19	
	HC236	187	UCAAGUCCUGCU AUACCCACCA	419	UGGUGGGUAUAG CAGGACUUGA	22	3′-t
	HC237	188	AGUCCUGCUAUA CCCACCA	420	UGGUGGGUAUAG CAGGACU	19	
$tRNA^{Lys\ (CUU)}$	HC238	189	CACCCUGUAGCU CAGAGGAAGA	421	UCUUCCUCUGAG CUACAGGGUG	22	5′-t
	HC239	190	CACCCUGUAGCU CAGAGGA	422	UCCUCUGAGCUA CAGGGUG	19	
	HC240	191	UCAAGUCCUACC AGGUUACCCA	423	UGGGUAACCUGG UAGGACUUGA	22	3′-t
	HC241	192	AGUCCUACCAGG UUACCCA	424	UGGGUAACCUGG UAGGACU	19	
$tRNA^{Gln\ (UUG)}\_2$	HC242	193	UGGAGUAUAGCC AAGUGGUAAG	425	CUUACCACUUGG CUAUACUCCA	22	5′-t
	HC243	194	UGGAGUAUAGCC AAGUGGU	426	ACCACUUGGCUAU ACUCCA	19	
	HC244	195	UCGAAUCCUUUU ACUCCAGCCA	427	UGGCUGGAGUAA AAGGAUUCGA	22	3′-t
	HC245	196	AAUCCUUUUACU CCAGCCA	428	UGGCUGGAGUAA AAGGAUU	19	
$tRNA^{Met\ (CAU)}\_3$	HC246	197	GGGCUUAUAGUU UAAUUGGUUG	429	CAACCAAUUAAAC UAUAAGCCC	22	5′-t
	HC247	198	GGGCUUAUAGUU UAAUUGG	430	CCAAUUAAACUAU AAGCCC	19	
	HC248	199	UCGAGCCCUACU AAGCCUACCA	431	UGGUAGGCUUAG UAGGGCUCGA	22	3′-t
	HC249	200	AGCCCUACUAAG CCUACCA	432	UGGUAGGCUUAG UAGGGCU	19	
$tRNA^{Met\ (CAU)}\_4$	HC250	201	GCAUCCAUGGCU GAAUGGUUAA	433	UUAACCAUUCAGC CAUGGAUGC	22	5′-t
	HC251	202	GCAUCCAUGGCU GAAUGGU	434	ACCAUUCAGCCAU GGAUGC	19	
	HC252	203	UCAAUUCCUACU GGAUGCACCA	435	UGGUGCAUCCAG UAGGAAUUGA	22	3′-t
	HC253	204	AUUCCUACUGGA UGCACCA	436	UGGUGCAUCCAG UAGGAAU	19	
$tRNA^{Tyr\ (GUA)}\_2$	HC254	205	GGGAGAGUGGCC GAGUGGUCAA	437	UUGACCACUCGG CCACUCUCCC	22	5′-t
	HC255	206	GGGAGAGUGGCC GAGUGGU	438	ACCACUCGGCCAC UCUCCC	19	
	HC256	207	UCGAAUCCUGCC UCUCCCACCA	439	UGGUGGGAGAGG CAGGAUUCGA	22	3′-t
	HC257	208	AAUCCUGCCUCU CCCACCA	440	UGGUGGGAGAGG CAGGAUU	19	
$tRNA^{Ser\ (GCU)}\_2$	HC258	209	GGAGGUAUGGCU GAGUGGCUUA	441	UAAGCCACUCAGC CAUACCUCC	22	5′-t
	HC259	210	GGAGGUAUGGCU GAGUGGC	442	GCCACUCAGCCAU ACCUCC	19	
	HC260	211	UCGAAUCCCAUU UCCUCCGCCA	443	UGGCGGAGGAAA UGGGAUUCGA	22	3′-t
	HC261	212	AAUCCCAUUUCC UCCGCCA	444	UGGCGGAGGAAA UGGGAUU	19	

TABLE 2-continued

RNA molecules derived from the sequences in Table 1 through artificial synthesis according to the present invention.

Source	Code	SEQ ID NO.	Sense sequence (5' to 3')	SEQ ID NO.	Antisense sequence (5' to 3')	Length (bp)	Group
$tRNA^{Phe(GAA)}$_3	HC262	213	GUUCAGGUAGCU CAGCUGGUUA	445	UAACCAGCUGAGC UACCUGAAC	22	5′-t
	HC263	214	GUUCAGGUAGCU CAGCUGG	446	CCAGCUGAGCUA CCUGAAC	19	
	HC264	215	UCGAAUCCACUU CUAAGCGCCA	447	UGGCGCUUAGAA GUGGAUUCGA	22	3′-t
	HC265	216	AAUCCACUUCUA AGCGCCA	448	UGGCGCUUAGAA GUGGAUU	19	
$tRNA^{Phe(AAA)}$	HC266	217	GUAACGAUCGAA UAAUGGAAGU	449	ACUUCCAUUAUUC GAUCGUUAC	22	5′-t
	HC267	218	GUAACGAUCGAA UAAUGGA	450	UCCAUUAUUCGAU CGUUAC	19	
	HC268	219	UCAAAUCCAAUU CGUUACUCCA	451	UGGAGUAACGAAU UGGAUUUGA	22	3′-t
	HC269	220	AAUCCAAUUCGU UACUCCA	452	UGGAGUAACGAAU UGGAUU	19	
$tRNA^{Pro(UGG)}$_3	HC270	221	AGGGAUGUAGCG CAGCUUGGUA	453	UACCAAGCUGCG CUACAUCCCU	22	5′-t
	HC271	222	AGGGAUGUAGCG CAGCUUG	454	CAAGCUGCGCUA CAUCCCU	19	
	HC272	223	UCCAAUCCUGUC AUCCCUACCA	455	UGGUAGGGAUGA CAGGAUUGGA	22	3′-t
	HC273	224	AAUCCUGUCAUC CCUACCA	456	UGGUAGGGAUGA CAGGAUU	19	
$tRNA^{Ile(CAU)}$	HC274	225	GGGCUAUUAGCU CAGUGGUAGA	457	UCUACCACUGAGC UAAUAGCCC	22	5′-t
	HC275	226	GGGCUAUUAGCU CAGUGGU	458	ACCACUGAGCUAA UAGCCC	19	
	HC276	227	UCAAGUCCAGGA UGGCCCACCA	459	UGGUGGGCCAUC CUGGACUUGA	22	3′-t
	HC277	228	AGUCCAGGAUGG CCCACCA	460	UGGUGGGCCAUC CUGGACU	19	
$tRNA^{Gly(GCC)}$_3	HC278	229	GCGGAAAUAGCU UAAUGGUAGA	461	UCUACCAUUAAGC UAUUUCCGC	22	5′-t
	HC279	230	GCGGAAAUAGCU UAAUGGU	462	ACCAUUAAGCUAU UUCCGC	19	
	HC280	231	UCAAGUCCCUCC UUCCGCUCCA	463	UGGAGCGGAAGG AGGGACUUGA	22	3′-t
	HC281	232	AGUCCCUCCUUC CGCUCCA	464	UGGAGCGGAAGG AGGGACU	19	

[0098] The inventors unexpectedly found that the RNA molecules isolated or derived from a plant of genus *Panax* in particular *Panax ginseng* C. A. Mey are effective on protecting cardiomyocytes, in particular they are capable of promoting the growth, proliferation and/or metastasis of cardiomyocytes.

[0099] Turning back to the method of treatment, the method comprises the step of administering an effective amount of RNA molecule as described above to the subject suffering from heart diseases. In an embodiment, the step of administering the RNA molecule to the subject comprises contacting cardiomyocytes of the subject with the RNA molecule.

[0100] The term "CHD" describes a physiological condition in subjects in which heart arteries are narrowed, less blood and oxygen reach the heart muscle. In an embodiment, the CHD to be treated is atherosclerosis, angina, heart attack and myocardial infarction. In a particular embodiment, the CHD is myocardial infarction. Accordingly, the method of the present invention can be applied to treat a subject suffering from a coronary heart disease and related disorders.

[0101] The term "subject" used herein refers to a living organism and can include but is not limited to a human and an animal. The subject is preferably a mammal, preferably a human. The RNA molecules may be administered through injection to the subject, preferably a human. The term injection encompasses intravenous, intramuscular, subcutaneous and intradermal administration. In an embodiment, the RNA molecule of the present invention is administered together with suitable excipient(s) to the subject through intravenous injection. For instance, the RNA molecule may be delivered to the subject or cells via transfection, electroporation or viral-mediated delivery.

[0102] The expression "effective amount" generally denotes an amount sufficient to produce therapeutically

desirable results, wherein the exact nature of the result varies depending on the specific condition which is treated. In this invention, CHD is the condition to be treated and therefore the result is usually a promotion or protection of the growth and proliferation of cardiomyocytes, a protection or amelioration of symptoms related to CHD. In an embodiment, where the injury is hypoxia/reoxygenation (ischemia/reperfusion) injury, the result is usually a promotion of the growth and proliferation of cardiomyocytes, relief of destruction of the cytoskeleton or amelioration of symptoms related to injured cardiomyocytes.

[0103] The RNA molecule of the present invention may be administered in form of a pharmaceutical composition comprising the RNA molecule and at least one pharmaceutically tolerable excipient. The pharmaceutically tolerable excipient may be one or more of a diluent, a filler, a binder, a disintegrant, a lubricant, a coloring agent, a surfactant, a gene delivery carrier and a preservative. The pharmaceutical composition can be present in solid, semisolid or liquid form, preferably in liquid form. The pharmaceutical composition can be liposome freeze-dried powder, polypeptide nanometer freeze-dried powder, spray and tablets. The pharmaceutical composition may comprise further pharmaceutical effective ingredients such as therapeutic compounds which are used for treating CHD such as Rg1. The skilled technician is able to select suitable pharmaceutically tolerable excipients depending on the form of the pharmaceutical composition and is aware of methods for manufacturing pharmaceutical compositions as well as able to select a suitable method for preparing the pharmaceutical composition depending on the kind of pharmaceutically tolerable excipients and the form of the pharmaceutical composition.

[0104] In an embodiment, RNA molecules provided as a composition containing a gene delivery vector. A gene delivery vector is any molecule that act as a carrier to deliver a gene to a cell. In embodiments where RNA molecules are transfected into cells, gene delivery vectors are considered to be transfection agents. In the embodiment of delivering RNA molecules by a recombinant viral vector, the gene delivery vector is a viral vector carrying a double-stranded RNA molecule describe above in the present invention. Gene delivery vectors include but are not limited to vectors such as virus vectors, collagens such as terminated peptide collagens, polymers such as polyetenimine (PEI), polypeptides such as poly (L-lysine) and protamine, and liposomes such as Lipofectamine. Gene delivery vectors can be commercially available, such as transfection reagents from Thermo Fisher, U.S.A. including Lipofectamine RNAiMAX, Lipofectamine 3000, Lipofectamine 2000 and DharmaFECT series from Dharmacon; RNAi-Mate from GenePharma, China; terminated peptide collagens from Koken Co. Ltd, Japan; and Histidine-lysine peptide copolymer from siRNAomics, China. Gene delivery vectors can be viral vectors based on retroviruses, adeno-associated viruses, adenoviruses, and lentiviruses. The gene delivery vector should be of low toxicity and not induce significant immune response in subjects. In an embodiment, the pharmaceutical composition may further comprise a nucleic acid stabilizer. The nucleic acid stabilizer refers to any chemicals that are capable of maintaining the stability of the RNA molecule in the composition to minimize or avoid degradation, in particular those having ability to deactivate activity of nucleases or the like degrading the RNA molecules.

[0105] Accordingly, the present invention also pertains to a pharmaceutical composition as described above, in particular comprising the RNA molecule and a pharmaceutically tolerable excipient as defined above. In an embodiment, the RNA molecule comprises at least one sequence selected from SEQ ID NO: 1 to 232 or a functional variant or homologue thereof.

[0106] Preferably, the RNA molecule is isolated or derived from a plant of the genus *Panax* as described above, in particular from *Panax ginseng* C. A. Mey.

[0107] The RNA molecules of the present invention are also suitable for promoting the growth and proliferation of cardiomyocytes. In another aspect of the invention, there is provided a method of promoting the growth and proliferation of cardiomyocytes comprising a step of contacting said cells with an effective amount of a RNA molecule as defined above. Preferably the RNA molecule is isolated or derived from a plant of the genus *Panax* or comprises a sequence selected from SEQ ID NO: 1 to SEQ ID NO: 232 or a functional variant or homologue thereof.

[0108] In an embodiment, the RNA molecule has a sequence length of from about 50 to 200 nucleotides, more preferably has a length of from about 60 to about 150 nucleotides, in particular from about 70 to about 100 nucleotides. The RNA molecule is a non-coding molecule preferably a transfer RNA molecule. Preferably, the RNA molecule comprises a sequence selected from SEQ ID NO: 465 to SEQ ID NO: 522 or a functional variant or homologue thereof; or the RNA molecule comprises SEQ ID NO: 465 to SEQ ID NO: 468 or a functional variant or homologue thereof; or the RNA molecule consists of a sequence selected from SEQ ID NO: 465 to SEQ ID NO: 522 or SEQ ID NO: 465 to SEQ ID NO: 468 or a functional variant or homologue thereof.

[0109] In an alternative embodiment, the RNA molecule has a sequence length of from about 10 to about 30 base pairs, from about 15 to about 25 base pairs, from about 19 to about 22 base pairs, 19 base pairs or 22 base pairs. Preferably, the RNA molecule is a double-stranded RNA molecule comprising a sense sequence selected from SEQ ID NO: 1 to SEQ ID NO: 232 or a functional variant or homologue thereof, in particular SEQ ID NO: 1 to SEQ ID NO: 40 or a functional variant or homologue thereof; or consists of a sequence selected from SEQ ID NO: 1 to SEQ ID NO: 232, in particular SEQ ID NO: 1 to SEQ ID NO: 40 or a functional variant or homologue thereof. The double-stranded RNA molecule comprises a complementary antisense sequence. The RNA molecule may further comprise 2 mer of 3' overhangs.

[0110] The step of contacting the cardiomyocytes with the RNA molecule of the present invention may be carried out by applying a composition in particular an incubation solution comprising the RNA molecule to said cardiomyocytes which incubation solution may further comprise suitable excipients as defined above, a buffer or a suitable growth medium. In such embodiment of the present invention, the cardiomyocytes are taken from a subject such as an animal or human, in particular a human. The RNA molecule is provided in the composition at a concentration of at least 0.3 nM, at least 3 nM, from about 0.3 nM to about 900 nM, from about 10 nM to about 100 nM, or from about 50 nM to about 300 nM. In addition, excipients may include gene delivery vectors, such as, but not limited to, collagen-based vectors or liposome formers.

[0111] In addition to the above, the present invention pertains to a double-stranded RNA molecule as described above, i.e. comprising a sense sequence selected from SEQ ID NO: 1 to SEQ ID NO: 232 or a functional variant or homologue thereof, and a complementary antisense sequence. In particular, the double-stranded RNA molecule consists of a sense sequence selected from SEQ ID NO: 1 to SEQ ID NO: 232 or a functional variant or homologue thereof, a complementary antisense sequence selected from SEQ ID NO: 233 to SEQ ID NO: 464, and optionally a 3' overhang. Example embodiments of the double-stranded RNA molecule are presented in Table 2. The double-stranded RNA may be subject to modification and therefore may carry at least one modified nucleoside selected form inosine, 1-methyladenosine, 2-methyladenosine, N^6-methyladenosine, N^6-isopentenyladenosine, 2'-O-methyladenosine, N^6-acetyladenosine, 1-methylinosine, pseudouridine, dihydrouridine, or 2-methylthio-N^6-methyladenosine.

[0112] In further aspect of the invention, there is provided a vector comprising a nucleic acid molecule, wherein the nucleic acid molecule is a RNA molecule as described above. In particular, the RNA molecule having a sequence selected from SEQ ID NO: 1 to SEQ ID NO: 232 or a functional variant or homologue thereof. In an embodiment, the vector is a recombinant vector comprising the double-stranded RNA molecule as described above. The vector may be viral-based vector derived from retrovirus, adeno-associated virus, adenovirus, or lentivirus. An ordinary skilled in the art would appreciate suitable approach to incorporate the RNA molecule of the present invention into a vector.

[0113] Still further, the present invention pertains to use of a nucleic acid molecule in the preparation of a medicament for treating CHD. The nucleic acid is a RNA molecule as described above including a functional variant or homologue thereof. It would also be appreciated that the RNA molecule of the present invention can be used as a small interfering RNA molecule to interfere the expression of certain genes in the target CHD, thereby to cause gene silencing, inhibition of apoptosis and injury, or the like to achieve the desired therapeutic effect.

[0114] Accordingly, the present invention provides a novel and effective approach for treating CHD from various origins by administration of a RNA molecule that is isolated or derived from a plant of the genus *Panax*, or in particular a RNA molecule comprising a sequence selected from SEQ ID NO: 1 to 232. Administration of said RNA molecule is also suitable for promoting the growth and proliferation of cardiomyocytes. The RNA molecules are found to be highly effective at promoting the growth and proliferation of cardiomyocytes in vitro.

[0115] The invention is now described in the following non-limiting examples.

EXAMPLES

Chemicals and Materials

[0116] Fresh roots of *Panax ginseng* C. A. Mey were collected from Fusong Town in the year of 2017 from Jilin Province, China. Cetrimonium bromide (CTAB) and sodium chloride were purchased from Kingdin Industrial Co., Ltd. (Hong Kong, China). Water-saturated phenol was purchased from Leagene Co., Ltd. (Beijing, China). Chloroform and ethanol were purchased from Anaqua Chemicals Supply Inc. Ltd. (U.S.A.). Isopentanol and guanidinium thiocyanate were purchased from Tokyo Chemical Industry CO., Ltd. (Japan). Tris-HCl and ethylenediaminetetraacetic acid (EDTA) were purchased from Acros Organics (U.S.A), low range ssRNA ladder was purchased from New England Biolabs (Beverly, Mass., U.S.A.). TRIzol® Reagent (Invitrogen), mirVana™ miRNA isolation kit, SYBR gold nucleic acid gel stain and gel loading buffer II were purchased from Thermo Fisher Scientific (U.S.A.). 40% acrylamide/bis solution (19:1), tris/borate/EDTA (TBE), ammonium persulphate (APS) and tetramethylethylenediamine (TEMED) were purchased from Biorad Laboratories Inc. (U.S.A). Rat cardiomyocyte cell line (H9C2) were purchased from ATCC (Manassas, Va., U.S.A.). Opti-MEM I Reduced Serum Media, Dulbecco's Modified Eagle Medium (DMEM), Glucose free Dulbecco's Modified Eagle Medium (glucose free DMEM), Fetal Bovine Serum (FBS), Penicillin-Streptomycin were purchased from Gibco (Life Technologies, Auckland, New Zealand). 3-(4,5-Dimethylthiazol-2-yl)-2,5-Diphenyltetrazolium Bromide (MTT) and DAPI was purchased from Sigma (St. Louis, Mo., U.S.A.). Mitochondrial viability stain solution was purchased from Abcam (Cambridge, England). Rhodamine Phalloidin was purchased from Cytoskeleton, Inc. (Denver, U.S.A.).

Example 1

[0117] Isolation of RNA molecules from a plant of genus *Panax* Roots of *Panax ginseng* C. A. Mey were freshly collected and immediately stored in liquid nitrogen until use. RNAs having a length of 200 nucleotides or below, i.e. small RNAs species, were extracted from *Panax ginseng* C. A. Mey by using a polysaccharase-aided RNA isolation (PARI) method, which method is described for the first time. Briefly, plant tissues were ground into a fine powder in liquid nitrogen and then homogenized in TRIzol reagent using a digital dispersing device (IKA, Germany). After fully lysed for 10 min at room temperature, an equal volume of chloroform was added and followed by centrifugation at 12,000×g for 15 min at 4° C. The supernatant was collected and precipitated by adding 1/25 volume of 5 M sodium chloride and 1.25 volume of cold absolute ethanol, and stored at −20° C. for 30 min. Then precipitation was hydrolyzed by polysaccharase, until the pellet was completely dissolved. The hydrolysate was mixed with 2×CTAB buffer, and extracted with an equal volume of phenol: chloroform:isopentanol (50:48:1) by vortexing vigorously. Phases were separated at 4° C. by centrifugation at 12,000×g for 15 min and the supernatant was extracted again as described above with chloroform:isopentanol (24:1). The supernatant was collected and mixed with an equal volume of 6 M guanidinium thiocyanate, followed by adding 100% ethanol to a final concentration of 55%. The mixture was passed through a filter cartridge containing a silica membrane, which immobilizes the RNAs. The filter was then washed for several times with 80% (v/v) ethanol solution, and finally all RNAs were eluted with a low ionic-strength solution or RNase-free water. The small RNA species were isolated and enriched by using a mirVana™ miRNA isolation kit following the manufacturer's instruction.

[0118] Further, the total tRNAs in the isolated small RNA species were separated by electrophoresis in 6% polyacrylamide TBE gels containing 8 M urea prepared according to the manufacturer's protocol (Biorad, U.S.A.). After staining with SYBR Gold nucleic acid gel stain, polyacrylamide gels were examined using a UV lamp and the region of gels

containing total tRNAs were cut off by using a clean and sharp scalpel. FIG. **1** shows gel electrophoresis profiles of small RNA species from *Panax ginseng* C. A. Mey, including low range ssRNA Ladder, small RNA molecules, transfer RNAs and individual transfer RNA including $tRNA^{Gly}_{(GCC)}$, $tRNA^{His(GUG)}$, $tRNA^{Met(CAU)}$. The band was sliced into small pieces and the total tRNAs were recovered from the gel by electroelution in a 3 kD molecular weight cut-off dialysis tubing (Spectrum, C.A.) at 100 V for 50 min in 1×TAE buffer. The eluents in the dialysis tubing were recovered and the total tRNAs were desalted and concentrated by using the mirVana™ miRNA isolation kit. The quality and purity of the RNA products were then confirmed using a Nanodrop Spectrophotometer (Thermo Scientific, U.S.A.) and Agilent 2100 Bioanalyzer (Agilent, U.S.A.).

[0119] The inventors then constructed the total tRNAs library and performed sequencing. Sequencing libraries were generated by using TruSeq small RNA Library Preparation Kit (Illumina, U.S.A.), followed by a round of adaptor ligation, reverse transcription and PCR enrichment. PCR products were then purified and libraries were quantified on the Agilent Bioanalyzer 2100 system (Agilent Technologies, U.S.A.). The library preparations were sequenced at the Novogene Bioinformatics Institute (Beijing, China) on an Illumina HiSeq platform using the 150 bp paired-end (PE150) strategy to generate over 15 million raw paired reads. U.S. Pat. No. 5,772,569 clean reads were obtained by removing low quality regions and adaptor sequences. FIG. **2** is a bar chart showing read length distribution of tRNAs. The tRNA genes were identified by using the tRNAscan-SE 2.0 program (http://lowelab.ucsc.edu/tRNAscan-SE/) and annotated by searching the Nucleotide Collection (nr/nt) database using Basic Local Alignment Search Tool (BLAST) program (https://blast.ncbi.nlm.nih.gov/Blast.cgi). 58 tRNA sequences from *Panax ginseng* C. A. Mey were identified and listed in Table 1.

[0120] Each of the tRNAs was then isolated from a mixture of small RNAs (<200 mer) from *Panax ginseng* C. A. Mey by immobilization of the target tRNAs onto the streptavidin-coated magnetic beads with specific biotinylated capture DNA probes. To bind specific tRNA molecules, a corresponded single stranded DNA oligonucleotide (20 to 45-mer) were synthesized, which was designed based on the sequence information of Illumina sequencing and should be complementary to a unique segment of the target tRNA. Cognate DNA probes were incubated with small RNA mixture for about 1.5 h in annealing buffer and allowed to hybridize to the targeted tRNA molecules in solution at the proper annealing temperatures that were generally 5° C. lower than the melting temperature (T_m). Streptavidin-coated magnetic beads were then added to the mixture and incubated for 30 min at the annealing temperatures. After the hybridized sequences are immobilized onto the magnetic beads via the streptavidin-biotin bond, the biotinylated DNA/tRNA coated beads were separated with a magnet for 1-2 min and washed 3-4 times in washing buffer at 40° C. The magnetic beads were resuspended to a desired concentration in RNase-free water and thereby to release the immobilized tRNA molecules by incubation at 70° C. for 5 min. Accordingly, the isolated and purified tRNA molecules of SEQ ID NO: 465 to 522 were obtained.

Example 2

Synthesis of RNA Molecules

[0121] The inventors designed and synthesized RNA molecules having a length of about 19 to 22 bp based on the 58 isolated tRNA sequences in Example 1. In particular, the tRNA sequences are considered to have at least 3 portions, namely a 5'-terminal portion (5'-t), a 3'-terminal portion (3'-t) and an anticodon portion. Each of the specifically designed RNA molecules contains any one of the portions. For instance, designed RNA molecules containing a 5' terminal portion of the corresponding full-length tRNA sequence are referred as 5'-t group RNA molecules; designed RNA molecules containing a 3' terminal portion of the corresponding full-length tRNA sequence are referred as 3'-t group RNA molecules; designed RNA molecules containing an anticodon portion of the corresponding full-length tRNA sequence are referred as anticodon group RNA molecules. The RNA molecules having a sense sequence selected from SEQ ID NO: 1 to SEQ ID NO: 232 and a complementary antisense sequence selected from SEQ ID NO: 233 to SEQ ID NO: 464, as shown in Table 2, were designed and synthesized by cleavage at different sites on the tRNA sequences in Table 1.

Example 3

Cardioprotective Effect of RNA Molecules on Cardiomyocytes

[0122] H9C2 cell lines were cultured in Dulbecco's Modified Eagle Medium (DMEM) containing 10% FBS and 1% penicillin/streptomycin at humidified atmosphere containing 5% CO_2 at 37° C.

[0123] In the cell viability assay or mitochondrial viability assay, exponentially growing cells of H9C2 cell line were plated in 96-well microplate at a density of 5000 cells per well in 100 μL of culture medium and allowed to adhere for 24 h before treatment. For hypoxia, hypoxic treatment was achieved by exposing cells to KRB buffer (composition in: NaCl 115 mM, KCl 4.7 mM, $CaCl_2$ 2.5 mM, KH_2PO_4 1.2 mM, $MgSO_4$ 1.2 mM, $NaHCO_3$ 24 mM, HEPES 10 mM; pH 7.4) at 37° C. for 3 hr in an oxygen-free hypoxic chamber (Stem Cell Technologies, United States), serial concentrations of RNA molecules obtained in Example 1 were then added to the cells before hypoxic treatment. For hypoxia/reoxygenation (H/R), Hypoxic treatment was achieved by exposing cells in glucose-free DMEM under conditions of 94.9% N_2/5% CO_2/0.1% O_2 for 12 hr at a hypoxystation (whitley H35 hypoxystation, Don Whitley Scientific Ltd., England), serial concentrations of RNA molecules obtained in Example 1 and 2 were then added to the cells and reoxygenation by incubating in the normoxic condition (95% air/5% CO_2) at 37° C. for 6 hr. After hypoxia or hypoxia/reoxygenation, MTT solution (100 μL per well, 0.5 mg/mL solution) or mitochondrial viability stain solution (follow the manufacture's instruction) was added to each well and incubated for 4 h at 37° C. Subsequently, for cell viability assay, 150 μL dimethyl sulfoxide (DMSO) were added and the optical densities of the resulting solutions were calorimetrically determined at 570 nm using a SpectraMax Paradigm multi-mode microplate reader (Molecular Devices, Sunnyvale, Calif., U.S.A). For mitochondrial viability assay, fluorescence detected at 550 nM excitation

and 590 nM emission using SpectraMax Paradigm multi-mode microplate reader. Dose-response curves were obtained and calculated by GraphPad Prism 6 (GraphPad, La Jolla, Calif., USA). Each experiment was carried out for three times and expressed as means±standard deviation.

[0124] With reference to FIG. **3**A, H9C2 cells were treated with 300 nM RNA molecules of $tRNA^{Gly(GCC)}$, $tRNA^{His(GUG)}$, $tRNA^{Met(CAU)}$ and $tRNA^{Leu(CAA)}$, i.e. SEQ ID NO: 465 to 468, and cultured under hypoxia before addition of MTT solution. The cell viability of these cells is compared to a control group and a hypoxia group. The results show that $tRNA^{Gly(GCC)}$, $tRNA^{Met(CAU)}$ and $tRNA^{Le(CAA)}$ are capable to promote the growth and proliferation of cardiomyocytes, indicating these RNA molecules can protect cardiomyocytes from hypoxic injury.

[0125] With reference to FIG. **3**B, H9C2 cells were treated with 50 nM RNA molecules of $tRNA^{Gly(GCC)}$, $tRNA^{His(GUG)}$, $tRNA^{Met(CAU)}$ and $tRNA^{Leu(CAA)}$, i.e. SEQ ID NO: 465 to 468, and cultured under hypoxia/reoxygenation before addition of MTT solution. The cell viability of these cells is compared to a control group and a H/R group. The results show that $tRNA^{Gly(GCC)}$, $tRNA^{His(GUG)}$ molecules are capable to promote the growth and proliferation of cardiomyocytes, indicating these RNA molecules can protect cardiomyocytes from hypoxia/reoxygenation (H/R) injury.

[0126] FIG. **4**A shows the cardioprotective effect of $tRNA^{His(GUG)}$, i.e. SEQ ID NO: 465, on H9C2 cells. Different concentrations of $tRNA^{His(GUG)}$ were used, i.e. 100 nM, 50 nM, 25 nM, and 12.5 nM, and compared to a control group and a H/R group. It is shown that the $tRNA^{His(GUG)}$ on cardiomyocytes in particular H9C2 cells exhibit significant cardioprotective effects in a dose-dependent manner.

[0127] FIG. **4**B shows the cardioprotective effect of $tRNA^{Gly(GCC)}$, i.e. SEQ ID NO: 466, on H9C2 cells. Different concentrations of $tRNA^{Gly(GCC)}$ were used, i.e. 100 nM, 50 nM, 25 nM, and 12.5 nM, and compared to a control group and a H/R group. It is shown that the $tRNA^{Gly(GCC)}$ on cardiomyocytes in particular H9C2 cells exhibit significant cardioprotective effects in a dose-dependent manner.

[0128] A comparative example of ginsenoside Rg1 implementation was used, and the results were shown in FIG. **4**C.

[0129] FIG. **5**A and FIG. **5**B show the cardioprotective effect of RNA molecules synthesized in Example 2 on H9C2 cells, in particular those having sense sequence of SEQ ID NO: 1 to 40. The results show that the RNA molecules HC50 and HC83 are effective in promoting the growth and proliferation of cardiomyocytes in particular H9C2 cells in this example. In other words, RNA molecules HC50 and HC83 are useful in protecting cardiomyocytes from hypoxia/reoxygenation (H/R) injury.

[0130] The inventors then specifically determined the cardioprotective effect of RNA molecule HC50 and HC83 on H9C2 cells, at different concentrations, i.e. 900 nM, 300 nM, 30 nM, 3 nM and 0.3 nM. As shown in FIG. **6**A, FIG. **6**B, FIG. **7**A and FIG. **7**B, the results are compared to a control group and a H/R group. The results demonstrated that RNA molecule HC50 and HC83 has a dose-dependent protective effect against hypoxia/reoxygenation (H/R) injury.

Example 4

Cytoskeleton Protection of RNA Molecules on Cardiomyocytes

[0131] H9C2 cells were plated in p-slide 8 well plate (Ibidi GmbH, Germany) at a density of 10000 cells per well in 200 μL of culture medium and allowed to adhere for 24 h before treatment. Hypoxic treatment was achieved by exposing cells in glucose-free DMEM under conditions of 94.9% N_2/5% CO_2/0.1% O_2 for 12 hr at a hypoxystation (whitley H35 hypoxystation, Don Whitley Scientific Ltd., England), serial concentrations of RNA molecules obtained in Example 2 were then added to the cells and reoxygenation by incubating in the normoxic condition (95% air/5% CO_2) at 37° C. for 6 hr. After hypoxia/reoxygenation, cells were stained with Rhodamine Phalloidin and DAPI following the manufacturer's instruction. Images were acquired on a Leica TCS SP8 Confocal Microscopy with a 20× objective.

[0132] The inventors specifically determined the protective effects of RNA molecule HC50 and HC83 on H9C2 cell cytoskeleton at different concentrations, i.e. 900 nM, 300 nM, 100 nM, 30 nM, 10 nM, 3 nM, and 0.3 nM. With reference to FIG. **8**A and FIG. **8**B, the results are compared to a control group and a H/R group. The cytoskeleton imaging showed RNA molecule HC50 and HC83 can significantly relieve cytoskeleton destruction of H9C2 cells caused by hypoxia/reoxygenation (H/R) injury in a dose-dependent manner.

[0133] Further, the inventors determined the protective effects of cholesterol-conjugated RNA molecule HC50 and HC83 on H9C2 cells at different concentrations, i.e. 900 nM, 300 nM, 100 nM, 30 nM, 10 nM, 3 nM, and 0.3 nM. With reference to FIG. **9**A and FIG. **9**B, the results are compared to a control group and a H/R group. The results showed that cholesterol-conjugated RNA molecule HC50 and HC83 has a dose-dependent protective effect against hypoxia/reoxygenation (H/R) injury. The inventors also determined the protective effects of cholesterol-conjugated RNA molecule HC50 and HC83 on H9C2 cell cytoskeleton at different concentrations, i.e. 900 nM, 300 nM, 100 nM, 30 nM, 10 nM, 3 nM, and 0.3 nM. With reference to FIG. **10**A and FIG. **10**B, the results are compared to a control group and a H/R group. The cytoskeleton imaging showed cholesterol-conjugated RNA molecule HC50 and HC83 can significantly relieve cytoskeleton destruction of H9C2 cells caused by hypoxia/reoxygenation (H/R) injury in a dose-dependent manner.

[0134] The inventors further compared the results to a control group and H/R along with DharmaFECT4 treated group (H/R+ DharmaFECT4), as shown in FIG. **11**A and FIG. **11**B, RNA molecule HC50 and HC83 promoted the growth and proliferation of cardiomyocytes against hypoxia/reoxygenation (H/R) injury in a dose-dependent manner.

[0135] Based on the above results, it is found that the small tRNA molecules isolated or derived from *Panax ginseng* C. A. Mey are highly effective on cardioprotection in vitro.

[0136] The embodiments described above are some examples of the present invention. For ordinary technicians in this field, several deformations and improvements can be made on the premise of not separating from the creative idea of the present invention, which belong to the protection scope of the present invention.

Numbered Embodiments

[0137] The implementation is further described with reference to the following numbered embodiments:

[0138] 1. A method of preventing or treating a subject suffering from heart disease comprising administering a transfer RNA molecule, a fragment derived from the transfer RNA molecule or a functional variant or homolog thereof, wherein the transfer RNA molecule is isolated from or derived from a plant of a genus *Panax*.

[0139] 2. The method of embodiment 1, wherein the plant of the genus *Panax* is *Panax ginseng* C. A. Mey, *Panax notoginseng* (Burkill) F. H. Chen or *Panax quinquefolius* Linn.

[0140] 3. The method of embodiment 1, wherein the transfer RNA molecule is a nucleic acid sequence selected from any one of SEQ ID NO: 465 to SEQ ID NO: 522.

[0141] 4. The method of embodiment 1, wherein the fragment derived from the transfer RNA molecule is a double-stranded RNA molecule comprising a sense sequence selected from any one of SEQ ID NO: 1 to SEQ ID NO: 232 or a functional variant or homolog thereof, and a complementary antisense sequence.

[0142] 5. The method of embodiment 1, wherein the transfer RNA molecule, the fragment derived from the transfer RNA molecule or the functional variant or homolog thereof comprises a 2 mer of 3' overhang.

[0143] 6. The method of embodiment 1, wherein the transfer RNA molecule, the fragment derived from the transfer RNA molecule or the functional variant or homolog thereof comprises a 3' cholesterol conjugation.

[0144] 7. The method of embodiment 1, wherein the transfer RNA molecule, the fragment derived from the transfer RNA molecule or the functional variant or homolog thereof comprises at least one modified nucleoside selected from inosine, 1-methyladenosine, 2-methyladenosine, N^6-methyladenosine, N^6-isopentenyladenosine, 2'-O-methyladenosine, N^6-acetyladenosine, 1-methylinosine, pseudouridine, dihydrouridine, or 2-methylthio-N^6-methyladenosine.

[0145] 8. The method of embodiment 1, wherein the heart disease is selected from one or more of angina pectoris, myocardial infarction, myocardial ischemic injury, coronary heart disease, cardiac hypertrophy, and myocardial fibrosis.

[0146] 9. A pharmaceutical composition for preventing or treating heart disease, wherein the pharmaceutical composition comprises an effective amount of a transfer RNA molecule, a fragment derived from the transfer RNA molecule or a functional variant or homolog thereof and a pharmaceutically tolerable vector, virus or excipient, wherein the transfer RNA molecule is isolated or derived from a plant of a genus *Panax*.

[0147] 10. The pharmaceutical composition of embodiment 9, wherein the plant of the genus *Panax* is *Panax ginseng* C. A. Mey, *Panax notoginseng* (Burkill) F. H. Chen or *Panax quinquefolius* Linn.

[0148] 11. The pharmaceutical composition of embodiment 9, wherein the transfer RNA molecule is a nucleic acid sequence selected from any one of SEQ ID NO: 465 to SEQ ID NO: 522.

[0149] 12. The pharmaceutical composition of embodiment 9, wherein the fragment derived from the transfer RNA molecule is a double-stranded RNA molecule comprising a sense sequence selected from any one of SEQ ID NO: 1 to SEQ ID NO: 232 or a functional variant or homolog thereof, and a complementary antisense sequence.

[0150] 13. The pharmaceutical composition of embodiment 9, wherein the transfer RNA molecule, the fragment derived from the transfer RNA molecule or the functional variant or homolog thereof comprises a 2 mer of 3' overhang.

[0151] 14. The pharmaceutical composition of embodiment 9, wherein the transfer RNA molecule, the fragment derived from the transfer RNA molecule or the functional variant or homolog thereof comprises a 3' cholesterol conjugation.

[0152] 15. The pharmaceutical composition of embodiment 9, wherein the transfer RNA molecule, the fragment derived from the transfer RNA molecule or the functional variant or homolog thereof comprises at least one modified nucleoside selected from inosine, 1-methyladenosine, 2-methyladenosine, N^6-methyladenosine, N^6-isopentenyladenosine, 2'-O-methyladenosine, N^6-acetyladenosine, 1-methylinosine, pseudouridine, dihydrouridine, or 2-methylthio-N^6-methyladenosine.

[0153] 16. The pharmaceutical composition of embodiment 9, wherein the heart disease is selected from one or more of angina pectoris, myocardial infarction, myocardial ischemic injury, coronary heart disease, cardiac hypertrophy, and myocardial fibrosis.

[0154] 17. A recombinant vector comprising a double-stranded RNA molecule, wherein the double-stranded RNA molecule comprises a sense sequence selected from any one of SEQ ID NO: 1 to SEQ ID NO: 232 or a functional variant or homolog thereof, and a complementary antisense sequence.

[0155] 18. The recombinant vector of embodiment 17, wherein the double-stranded RNA molecule comprises a 2 mer of 3' overhang.

[0156] 19. The recombinant vector of embodiment 17, wherein the double-stranded RNA molecule comprises a 3' cholesterol conjugation.

[0157] 20. The recombinant vector of embodiment 17, wherein the double-stranded RNA molecule comprises at least one modified nucleoside selected from inosine, 1-methyladenosine, 2-methyladenosine, N^6-methyladenosine, N^6-isopentenyladenosine, 2'-O-methyladenosine, N^6-acetyladenosine, 1-methyl inosine, pseudouridine, dihydrouridine, or 2-methylthio-N^6-methyladenosine.

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gcaccagugg ucuaguggua ga 22

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uuucccggcu ggugcacca 19

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gucguuguag uauaguggua ag 22

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gucguuguag uauaguggu 19

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ggggauguag cucagaugg 19

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gguuucgugg uguaguuggu ua 22

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gguuucgugg uguaguugg 19

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gucugggugg uguagucggu ua 22

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ucgaacccgg gcucagacac ca 22

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aacccgggcu cagacacca 19

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ggauggaugu cugagcgguu gg 22

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uugauccacg uucaccgcac ca 22

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auccacguuc accgcacca 19

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gcauccaugg cugaaugguu aa 22

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auuccuacug gaugcacca 19

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aaucccgggc aacccacca 19

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ucgaaucccu cucucuccuc ca 22

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aggagagaug gccgaguggu ug 22

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aggagagaug gccgagugg 19

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gcggguauag uuuaguggua aa 22

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ucgauucccg cuacccgcuc ca 22

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auucccgcua cccgcucca 19

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gcguccauug ucuaauggau ag 22

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gcguccauug ucuaaugga 19

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ucaaauccua uuggacgcac ca 22

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gggccuguag cucagaggau ua 22

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gggccuguag cucagagga 19

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ucgaaucccu ccucgcccac ca 22

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aaucccuccu cgcccacca 19

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ggcgauaugg ccgaguggua ag 22

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ucaaauccga uaaggggcuc ca 22

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gccugcuuag cucagagguu ag 22

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gccugcuuag cucagaggu 19

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accuacuuaa cucagugguu ag 22

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accuacuuaa cucaguggu 19

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ucaaauccaa uaguagguac ca 22

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<400> SEQUENCE: 152

aauccaauag uagguacca 19

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<400> SEQUENCE: 153

ggggauaugg cggaauuggu ag 22

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ggggauaugg cggaauugg 19

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ucaagucccu cuaucccccac ca 22

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agucccucua uccccacca 19

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gggcuuauag uuuaauuggu ug 22

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ggagguaugg cugaguggcu ua 22

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guucagguag cucagcuggu ua 22

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guaacgaucg aauaauggaa gu 22

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gcggaaauag cuuaauggua ga 22

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accauucgac uauauccgc 19

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uggugccuug aagaggacu 19

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caaacugcuc uacuccgcg 19

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uccacucagc caucucucc 19

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uugaccauua cucuaccccg cu 22

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accgcucaga cauccaucc 19

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caaccacucg gccaucucuc cu 22

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ccacucggcc aucucuccu 19

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cuaaccucug agcuaagcag gc 22

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cuaccaauuc cgccauaucc cc 22

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ccaauuccgc cauaucccc 19

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cuaccgauuu caccauagcg gc 22

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ugguagggcu auacggacu 19

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cgaacugaac uaagagcgc 19

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ugguggagau aagcggacu 19

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ccaacugagc uauacaccc 19

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ugguggguau agcaggacuu ga 22

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uccucugagc uacagggug 19

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cuuaccacuu ggcuauacuc ca 22

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caaccaauua aacuauaagc cc 22

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ccaauuaaac uauaagccc 19

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ugguaggcuu aguagggcu 19

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accauucagc cauggaugc 19

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uggugcaucc aguaggaauu ga 22

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uugaccacuc ggccacucuc cc 22

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accacucggc cacucuccc 19

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uggcggagga aaugggauu 19

<210> SEQ ID NO 445
<211> LENGTH: 22
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Artificially synthesized

<400> SEQUENCE: 445

uaaccagcug agcuaccuga ac 22

<210> SEQ ID NO 446
<211> LENGTH: 19
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Artificially synthesized

<400> SEQUENCE: 446

ccagcugagc uaccugaac 19

<210> SEQ ID NO 447
<211> LENGTH: 22
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Artificially synthesized

<400> SEQUENCE: 447

uggcgcuuag aaguggauuc ga 22

<210> SEQ ID NO 448
<211> LENGTH: 19
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Artificially synthesized

<400> SEQUENCE: 448

uggcgcuuag aaguggauu 19

<210> SEQ ID NO 449
<211> LENGTH: 22
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Artificially synthesized

<400> SEQUENCE: 449

acuuccauua uucgaucguu ac 22

<210> SEQ ID NO 450
<211> LENGTH: 19
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Artificially synthesized

<400> SEQUENCE: 450

uccauuauuc gaucguuac 19

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<210> SEQ ID NO 451
<211> LENGTH: 22
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Artificially synthesized

<400> SEQUENCE: 451

uggaguaacg aauuggauuu ga 22

<210> SEQ ID NO 452
<211> LENGTH: 19
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Artificially synthesized

<400> SEQUENCE: 452

uggaguaacg aauuggauu 19

<210> SEQ ID NO 453
<211> LENGTH: 22
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Artificially synthesized

<400> SEQUENCE: 453

uaccaagcug cgcuacaucc cu 22

<210> SEQ ID NO 454
<211> LENGTH: 19
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Artificially synthesized

<400> SEQUENCE: 454

caagcugcgc uacaucccu 19

<210> SEQ ID NO 455
<211> LENGTH: 22
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Artificially synthesized

<400> SEQUENCE: 455

ugguagggau gacaggauug ga 22

<210> SEQ ID NO 456
<211> LENGTH: 19
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Artificially synthesized

<400> SEQUENCE: 456

ugguagggau gacaggauu 19

<210> SEQ ID NO 457
<211> LENGTH: 22
<212> TYPE: RNA

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<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Artificially synthesized

<400> SEQUENCE: 457

ucuaccacug agcuaauagc cc 22

<210> SEQ ID NO 458
<211> LENGTH: 19
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Artificially synthesized

<400> SEQUENCE: 458

accacugagc uaauagccc 19

<210> SEQ ID NO 459
<211> LENGTH: 22
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Artificially synthesized

<400> SEQUENCE: 459

uggugggcca uccuggacuu ga 22

<210> SEQ ID NO 460
<211> LENGTH: 19
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Artificially synthesized

<400> SEQUENCE: 460

uggugggcca uccuggacu 19

<210> SEQ ID NO 461
<211> LENGTH: 22
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Artificially synthesized

<400> SEQUENCE: 461

ucuaccauua agcuauuucc gc 22

<210> SEQ ID NO 462
<211> LENGTH: 19
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Artificially synthesized

<400> SEQUENCE: 462

accauuaagc uauuuccgc 19

<210> SEQ ID NO 463
<211> LENGTH: 22
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Artificially synthesized

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<400> SEQUENCE: 463

uggagcggaa ggagggacuu ga 22

<210> SEQ ID NO 464
<211> LENGTH: 19
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Artificially synthesized

<400> SEQUENCE: 464

uggagcggaa ggagggacu 19

<210> SEQ ID NO 465
<211> LENGTH: 77
<212> TYPE: RNA
<213> ORGANISM: Panax ginseng

<400> SEQUENCE: 465

gcggauguag ccaaguggau caaggcagug gauugugaau ccaccaugcg cggguucaau 60

ucccgucguu cgcccca 77

<210> SEQ ID NO 466
<211> LENGTH: 74
<212> TYPE: RNA
<213> ORGANISM: Panax ginseng

<400> SEQUENCE: 466

gcggauauag ucgaauggua aaauuucucu uugccaagga gaagacgcgg guucgauucc 60

cgcuauccgc ccca 74

<210> SEQ ID NO 467
<211> LENGTH: 84
<212> TYPE: RNA
<213> ORGANISM: Panax ginseng

<400> SEQUENCE: 467

gccuuggugg ugaaauggua gacacgcgag acucaaaauc ucgugcuaaa gagcguggag 60

guucgagucc ucuucaaggc acca 84

<210> SEQ ID NO 468
<211> LENGTH: 77
<212> TYPE: RNA
<213> ORGANISM: Panax ginseng

<400> SEQUENCE: 468

cgcggaguag agcaguuugg uagcucgcaa ggcucauaac cuugagguca cggguucaaa 60

uccugucucc gcaacca 77

<210> SEQ ID NO 469
<211> LENGTH: 77
<212> TYPE: RNA
<213> ORGANISM: Panax ginseng

<400> SEQUENCE: 469

gggauuguag uucaaucggu cagagcaccg cccugucaag gcggaagcug cggguucgag 60

ccccgucagu cccgcca 77

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<210> SEQ ID NO 470
<211> LENGTH: 91
<212> TYPE: RNA
<213> ORGANISM: Panax ginseng

<400> SEQUENCE: 470

ggagagaugg cugaguggac uaaagcggcg gauugcuaau ccgcuguacg aguuauucgu 60

accgaggguu cgaaucccuc ucuuuccgcc a 91

<210> SEQ ID NO 471
<211> LENGTH: 75
<212> TYPE: RNA
<213> ORGANISM: Panax ginseng

<400> SEQUENCE: 471

uggggcgugg ccaaguggua aggcaacggg uuuuggcccc gcuauucgga gguucgaauc 60

cuuccguccc agcca 75

<210> SEQ ID NO 472
<211> LENGTH: 76
<212> TYPE: RNA
<213> ORGANISM: Panax ginseng

<400> SEQUENCE: 472

gcccccaucg ucuaguggguu caggacaucu cucuuucaag gaggcagcgg ggauucgacu 60

uccccugggg guacca 76

<210> SEQ ID NO 473
<211> LENGTH: 75
<212> TYPE: RNA
<213> ORGANISM: Panax ginseng

<400> SEQUENCE: 473

uccucaguag cucaguggua gagcggucgg cuguuaacug acuggucgua gguucgaauc 60

cuaccugggg agcca 75

<210> SEQ ID NO 474
<211> LENGTH: 77
<212> TYPE: RNA
<213> ORGANISM: Panax ginseng

<400> SEQUENCE: 474

agggauguag cgcagcuugg uagcgcuuuu guuuugggua caaaauguca cggguucaaa 60

uccugucauc ccuacca 77

<210> SEQ ID NO 475
<211> LENGTH: 75
<212> TYPE: RNA
<213> ORGANISM: Panax ginseng

<400> SEQUENCE: 475

gguuccaugg ucuagugguc aggacauugg acucugaauc caguaacccg aguucagguc 60

ucgguggaac cucca 75

<210> SEQ ID NO 476
<211> LENGTH: 75
<212> TYPE: RNA

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<213> ORGANISM: Panax ginseng

<400> SEQUENCE: 476

uccguugucg uccagcgguu aggauaucug gcuuucaccc aggagacccg gguucguuuc 60

ccggcaacgg aacca 75

<210> SEQ ID NO 477
<211> LENGTH: 74
<212> TYPE: RNA
<213> ORGANISM: Panax ginseng

<400> SEQUENCE: 477

ggcuagguaa cauaauggaa auguauugga cugcaaaucc uggaaugacg guucgacccc 60

guccuuggcc ucca 74

<210> SEQ ID NO 478
<211> LENGTH: 76
<212> TYPE: RNA
<213> ORGANISM: Panax ginseng

<400> SEQUENCE: 478

agcgggguag aguaaugguc aacucaucag ucucauuauc ugaagacuac agguucgaau 60

ccugucccg ccucca 76

<210> SEQ ID NO 479
<211> LENGTH: 78
<212> TYPE: RNA
<213> ORGANISM: Panax ginseng

<400> SEQUENCE: 479

cgagguguag cgcagucugg ucagcgcauc uguuuugggu acagagggcc auagguucga 60

auccugucac cuugacca 78

<210> SEQ ID NO 480
<211> LENGTH: 74
<212> TYPE: RNA
<213> ORGANISM: Panax ginseng

<400> SEQUENCE: 480

gcaccagugg ucuaguggua gaauaguacc cugccacggu acagacccgg guucguuucc 60

cggcuggugc acca 74

<210> SEQ ID NO 481
<211> LENGTH: 75
<212> TYPE: RNA
<213> ORGANISM: Panax ginseng

<400> SEQUENCE: 481

gucguuguag uauaguggua aguauucccg ccugucacgc gggugacccg gguucgaucc 60

ccggcaacgg cgcca 75

<210> SEQ ID NO 482
<211> LENGTH: 89
<212> TYPE: RNA
<213> ORGANISM: Panax ginseng

<400> SEQUENCE: 482

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ccgaccuuag cucaguuggu agagcggagg acuguagugu gcucguagcu auccuuaggu 60

cgcugguucg aauccggcug gucggacca 89

<210> SEQ ID NO 483
<211> LENGTH: 76
<212> TYPE: RNA
<213> ORGANISM: Panax ginseng

<400> SEQUENCE: 483

ggggauguag cucagauggu agagcgcucg cuuagcaugc gagagguacg gggaucgaua 60

ccccgcaucu ccacca 76

<210> SEQ ID NO 484
<211> LENGTH: 76
<212> TYPE: RNA
<213> ORGANISM: Panax ginseng

<400> SEQUENCE: 484

uccguuguag ucuaguuggu caggauacuc ggcucucacc cgagagaccc ggguucaagu 60

cccggcaacg gaacca 76

<210> SEQ ID NO 485
<211> LENGTH: 75
<212> TYPE: RNA
<213> ORGANISM: Panax ginseng

<400> SEQUENCE: 485

gucccuuucg uccagugguu aggacaucgu cuuuucaugu cgaagacacg gguucgauuc 60

ccguaagggg uacca 75

<210> SEQ ID NO 486
<211> LENGTH: 76
<212> TYPE: RNA
<213> ORGANISM: Panax ginseng

<400> SEQUENCE: 486

gcgccuguag cucaguggau agagcgucug uuuccuaagc agaaagucgu agguucgacc 60

ccuaccuggc gcgcca 76

<210> SEQ ID NO 487
<211> LENGTH: 77
<212> TYPE: RNA
<213> ORGANISM: Panax ginseng

<400> SEQUENCE: 487

gguuucgugg uguaguuggu uaucacguca gccuaacaca cugaaggucu ccgguucgaa 60

cccgggcgaa gccacca 77

<210> SEQ ID NO 488
<211> LENGTH: 77
<212> TYPE: RNA
<213> ORGANISM: Panax ginseng

<400> SEQUENCE: 488

gucugggugg uguagucggu uaucaugcua gucucacaca cuagaggucc ccgguucgaa 60

cccgggcuca gacacca 77

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<210> SEQ ID NO 489
<211> LENGTH: 90
<212> TYPE: RNA
<213> ORGANISM: Panax ginseng

<400> SEQUENCE: 489

ggauggaugu cugagcgguu ggaagagucg gucuugaaaa ccgaaguauu gauaggaaua 60

ccggggguuc gaaucccucu ccauccgcca 90

<210> SEQ ID NO 490
<211> LENGTH: 76
<212> TYPE: RNA
<213> ORGANISM: Panax ginseng

<400> SEQUENCE: 490

gcggggauag cucaguuggg agagugucag acugaagauc uaaaggucac guguuugauc 60

cacguucacc gcacca 76

<210> SEQ ID NO 491
<211> LENGTH: 77
<212> TYPE: RNA
<213> ORGANISM: Panax ginseng

<400> SEQUENCE: 491

gcauccaugg cugaaugguu aaagcgccca acucauaauu ggcgaauucg uagguucaau 60

uccuacugga ugcacca 77

<210> SEQ ID NO 492
<211> LENGTH: 75
<212> TYPE: RNA
<213> ORGANISM: Panax ginseng

<400> SEQUENCE: 492

ggguugcuaa cucaacggua gaguacucgg cuuuuaaccg acuaguuccg gguucgaauc 60

ccgggcaacc cacca 75

<210> SEQ ID NO 493
<211> LENGTH: 95
<212> TYPE: RNA
<213> ORGANISM: Panax ginseng

<400> SEQUENCE: 493

ggagagaugg cugagugguu gauagcuccg gucuugaaaa ccggcauagu uuuaacaaag 60

aacuaucgag gguucgaauc ccucucucuc cucca 95

<210> SEQ ID NO 494
<211> LENGTH: 91
<212> TYPE: RNA
<213> ORGANISM: Panax ginseng

<400> SEQUENCE: 494

aggagagaug gccgaguggu ugaaggcgua gcauuggaac ugcuauguag gcuuuuguuu 60

accgaggguu cgaaucccuc ucuuuccgcc a 91

<210> SEQ ID NO 495
<211> LENGTH: 74
<212> TYPE: RNA

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<213> ORGANISM: Panax ginseng

<400> SEQUENCE: 495

gcggguauag uuuaguggua aaacccuagc cuuccaagcu aacgaugcgg guucgauucc 60

cgcuacccgc ucca 74

<210> SEQ ID NO 496
<211> LENGTH: 75
<212> TYPE: RNA
<213> ORGANISM: Panax ginseng

<400> SEQUENCE: 496

gcguccauug ucuaauggau aggacagagg ucuucuaaac cuuugguaua gguucaaauc 60

cuauuggacg cacca 75

<210> SEQ ID NO 497
<211> LENGTH: 77
<212> TYPE: RNA
<213> ORGANISM: Panax ginseng

<400> SEQUENCE: 497

gggccuguag cucagaggau uagagcacgu ggcuacgaac cacggugucg gggguucgaa 60

ucccuccucg cccacca 77

<210> SEQ ID NO 498
<211> LENGTH: 75
<212> TYPE: RNA
<213> ORGANISM: Panax ginseng

<400> SEQUENCE: 498

ggcgauaugg ccgaguggua aggcggggga cugcaaaucc uuuuuucccc aguucaaauc 60

cgggugucgc cucca 75

<210> SEQ ID NO 499
<211> LENGTH: 87
<212> TYPE: RNA
<213> ORGANISM: Panax ginseng

<400> SEQUENCE: 499

gggucgaugc ccgagcgguu aaugggggacg gacuguaaau ucguuggcaa uaugucuacg 60

cugguucaaa uccagcucgg cccacca 87

<210> SEQ ID NO 500
<211> LENGTH: 75
<212> TYPE: RNA
<213> ORGANISM: Panax ginseng

<400> SEQUENCE: 500

gcccuuuuaa cucagcggua gaguaacgcc augguaaggc guaagucauc gguucaaauc 60

cgauaagggg cucca 75

<210> SEQ ID NO 501
<211> LENGTH: 76
<212> TYPE: RNA
<213> ORGANISM: Panax ginseng

<400> SEQUENCE: 501

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gccugcuuag cucagagguu agagcaucgc auuuguaaug cgauggucau cgguucgauu 60

ccgauagccg gcucca 76

<210> SEQ ID NO 502
<211> LENGTH: 76
<212> TYPE: RNA
<213> ORGANISM: Panax ginseng

<400> SEQUENCE: 502

accuacuuaa cucaguggguu agaguauugc uuucauacgg cgggagucau ugguucaaau 60

ccaauaguag guacca 76

<210> SEQ ID NO 503
<211> LENGTH: 87
<212> TYPE: RNA
<213> ORGANISM: Panax ginseng

<400> SEQUENCE: 503

ggggauaugg cggaauuggu agacgcuacg gacuuaaaau ccgucgacuu uaaaaucgug 60

aggguucaag ucccucuauc cccacca 87

<210> SEQ ID NO 504
<211> LENGTH: 83
<212> TYPE: RNA
<213> ORGANISM: Panax ginseng

<400> SEQUENCE: 504

gccgcuaugg ugaaaucggu agacacgcug cucuuaggaa gcagugcuag agcaucucgg 60

uucgaguccg aguggcggca cca 83

<210> SEQ ID NO 505
<211> LENGTH: 76
<212> TYPE: RNA
<213> ORGANISM: Panax ginseng

<400> SEQUENCE: 505

gucgggauag cucagcuggu agagcagagg acugaaaauc cucgugucac caguucaaau 60

cugguuccug gcacca 76

<210> SEQ ID NO 506
<211> LENGTH: 77
<212> TYPE: RNA
<213> ORGANISM: Panax ginseng

<400> SEQUENCE: 506

agggcuauag cucaguuagg uagagcaccu cguuuacacc gagaaggucu acgguccgag 60

uccguauagc ccuacca 77

<210> SEQ ID NO 507
<211> LENGTH: 75
<212> TYPE: RNA
<213> ORGANISM: Panax ginseng

<400> SEQUENCE: 507

agggauauaa cucagcggua gagugucacc uugacguggu ggaagucauc aguucgagcc 60

ugauuauccc uacca 75

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<210> SEQ ID NO 508
<211> LENGTH: 77
<212> TYPE: RNA
<213> ORGANISM: Panax ginseng

<400> SEQUENCE: 508

gcgcucuuag uucaguucgg uagaacgugg gucuccaaaa cccaaugucg uagguucaaa 60

uccuacagag cgugcca 77

<210> SEQ ID NO 509
<211> LENGTH: 75
<212> TYPE: RNA
<213> ORGANISM: Panax ginseng

<400> SEQUENCE: 509

gggcuauuag cucaguggua gagcgcgccc cugauaaggg cgaggucucu gguucaaguc 60

caggauggcc cacca 75

<210> SEQ ID NO 510
<211> LENGTH: 76
<212> TYPE: RNA
<213> ORGANISM: Panax ginseng

<400> SEQUENCE: 510

ggggauauag cucaguuggu agagcuccgc ucuugcaagg cggaugucag cgguucgagu 60

ccgcuuaucu ccacca 76

<210> SEQ ID NO 511
<211> LENGTH: 76
<212> TYPE: RNA
<213> ORGANISM: Panax ginseng

<400> SEQUENCE: 511

ggguguauag cucaguuggu agagcauugg gcuuuuaacc uaauggucgc agguucaagu 60

ccugcuauac ccacca 76

<210> SEQ ID NO 512
<211> LENGTH: 75
<212> TYPE: RNA
<213> ORGANISM: Panax ginseng

<400> SEQUENCE: 512

cacccuguag cucagaggaa gaguggucgu cucuuagcug acaggucgua gguucaaguc 60

cuaccagguu accca 75

<210> SEQ ID NO 513
<211> LENGTH: 67
<212> TYPE: RNA
<213> ORGANISM: Panax ginseng

<400> SEQUENCE: 513

uggaguauag ccaaguggua aggcaccggu uuuugguacc gagguucgaa uccuuuuacu 60

ccagcca 67

<210> SEQ ID NO 514
<211> LENGTH: 77
<212> TYPE: RNA

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<213> ORGANISM: Panax ginseng

<400> SEQUENCE: 514

gggcuuauag uuuaauuggu ugaaacguac cgcucauaac gguuauauug uagguucgag 60

cccuacuaag ccuacca 77

<210> SEQ ID NO 515
<211> LENGTH: 77
<212> TYPE: RNA
<213> ORGANISM: Panax ginseng

<400> SEQUENCE: 515

gcauccaugg cugaaugguu aaagcgccca acucauaauu ggcgaauucg uagguucaau 60

uccuacugga ugcacca 77

<210> SEQ ID NO 516
<211> LENGTH: 86
<212> TYPE: RNA
<213> ORGANISM: Panax ginseng

<400> SEQUENCE: 516

gggagagugg ccgagugguc aaaagcgaca gacuguaaau cuguugaagu uuuucuacgu 60

agguucgaau ccugccucuc ccacca 86

<210> SEQ ID NO 517
<211> LENGTH: 91
<212> TYPE: RNA
<213> ORGANISM: Panax ginseng

<400> SEQUENCE: 517

ggagguaugg cugaguggcu uaaggcauug guuugcuaaa ucgacauaca agaagauugu 60

aucauggguu cgaaucccau uuccuccgcc a 91

<210> SEQ ID NO 518
<211> LENGTH: 77
<212> TYPE: RNA
<213> ORGANISM: Panax ginseng

<400> SEQUENCE: 518

guucagguag cucagcuggu uagagcaaag gacugaaaau ccuuguguca gugguucgaa 60

uccacuucua agcgcca 77

<210> SEQ ID NO 519
<211> LENGTH: 78
<212> TYPE: RNA
<213> ORGANISM: Panax ginseng

<400> SEQUENCE: 519

guaacgaucg aauaauggaa guucacgggg aaagucacua gacccgaagc auugguucaa 60

auccaauucg uuacucca 78

<210> SEQ ID NO 520
<211> LENGTH: 82
<212> TYPE: RNA
<213> ORGANISM: Panax ginseng

<400> SEQUENCE: 520

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agggauguag cgcagcuugg uagcgccuuu guuuugggua aaaaauguca cggguuccaa 60

uccaauccug ucaucccuac ca 82

<210> SEQ ID NO 521
<211> LENGTH: 75
<212> TYPE: RNA
<213> ORGANISM: Panax ginseng

<400> SEQUENCE: 521

gggcuauuag cucaguggua gagcgcgccc cugauaaggg cgaggucucu gguucaaguc 60

caggauggcc cacca 75

<210> SEQ ID NO 522
<211> LENGTH: 75
<212> TYPE: RNA
<213> ORGANISM: Panax ginseng

<400> SEQUENCE: 522

gcggaaauag cuuaauggua gagcauagcc uugccaaggc ugagguugag gguucaaguc 60

ccuccuuccg cucca 75

What is claimed is:

1. A method of preventing or treating a subject suffering from heart disease comprising administering a transfer RNA molecule, a fragment derived from the transfer RNA molecule or a functional variant or homolog thereof, wherein the transfer RNA molecule is isolated from or derived from a plant of a genus *Panax*.

2. The method of claim **1**, wherein the plant of the genus *Panax* is *Panax ginseng* C. A. Mey, *Panax notoginseng* (Burkill) F. H. Chen or *Panax quinquefolius* Linn.

3. The method of claim **1**, wherein the transfer RNA molecule is a nucleic acid sequence selected from any one of SEQ ID NO: 465 to SEQ ID NO: 522.

4. The method of claim **1**, wherein the fragment derived from the transfer RNA molecule is a double-stranded RNA molecule comprising a sense sequence selected from any one of SEQ ID NO: 1 to SEQ ID NO: 232 or a functional variant or homolog thereof, and a complementary antisense sequence.

5. The method of claim **1**, wherein the transfer RNA molecule, the fragment derived from the transfer RNA molecule or the functional variant or homolog thereof comprises a 2 mer of 3' overhang.

6. The method of claim **1**, wherein the transfer RNA molecule, the fragment derived from the transfer RNA molecule or the functional variant or homolog thereof comprises a 3' cholesterol conjugation.

7. The method of claim **1**, wherein the transfer RNA molecule, the fragment derived from the transfer RNA molecule or the functional variant or homolog thereof comprises at least one modified nucleoside selected from inosine, 1-methyladenosine, 2-methyladenosine, N^6-methyladenosine, N^6-isopentenyladenosine, 2'-O-methyladenosine, N^6-acetyladenosine, 1-methylinosine, pseudouridine, dihydrouridine, or 2-methylthio-N^6-methyladenosine.

8. The method of claim **1**, wherein the heart disease is selected from one or more of angina pectoris, myocardial infarction, myocardial ischemic injury, coronary heart disease, cardiac hypertrophy, and myocardial fibrosis.

9. A pharmaceutical composition for preventing or treating heart disease, wherein the pharmaceutical composition comprises an effective amount of a transfer RNA molecule, a fragment derived from the transfer RNA molecule or a functional variant or homolog thereof and a pharmaceutically tolerable vector, virus or excipient, wherein the transfer RNA molecule is isolated or derived from a plant of a genus *Panax*.

10. The pharmaceutical composition of claim **9**, wherein the plant of the genus *Panax* is *Panax ginseng* C. A. Mey, *Panax notoginseng* (Burkill) F. H. Chen or *Panax quinquefolius* Linn.

11. The pharmaceutical composition of claim **9**, wherein the transfer RNA molecule is a nucleic acid sequence selected from any one of SEQ ID NO: 465 to SEQ ID NO: 522.

12. The pharmaceutical composition of claim **9**, wherein the fragment derived from the transfer RNA molecule is a double-stranded RNA molecule comprising a sense sequence selected from any one of SEQ ID NO: 1 to SEQ ID NO: 232 or a functional variant or homolog thereof, and a complementary antisense sequence.

13. The pharmaceutical composition of claim **9**, wherein the transfer RNA molecule, the fragment derived from the transfer RNA molecule or the functional variant or homolog thereof comprises a 2 mer of 3' overhang.

14. The pharmaceutical composition of claim **9**, wherein the transfer RNA molecule, the fragment derived from the transfer RNA molecule or the functional variant or homolog thereof comprises a 3' cholesterol conjugation.

15. The pharmaceutical composition of claim **9**, wherein the transfer RNA molecule, the fragment derived from the transfer RNA molecule or the functional variant or homolog thereof comprises at least one modified nucleoside selected from inosine, 1-methyladenosine, 2-methyladenosine, N^6-methyladenosine, N^6-isopentenyladenosine, 2'-O-meth-

yladenosine, N^6-acetyladenosine, 1-methyl inosine, pseudouridine, dihydrouridine, or 2-methylthio-N^6-methyl-adenosine.

16. The pharmaceutical composition of claim **9**, wherein the heart disease is selected from one or more of angina pectoris, myocardial infarction, myocardial ischemic injury, coronary heart disease, cardiac hypertrophy, and myocardial fibrosis.

17. A recombinant vector comprising a double-stranded RNA molecule, wherein the double-stranded RNA molecule comprises a sense sequence selected from any one of SEQ ID NO: 1 to SEQ ID NO: 232 or a functional variant or homolog thereof, and a complementary antisense sequence.

18. The recombinant vector of claim **17**, wherein the double-stranded RNA molecule comprises a 2 mer of 3' overhang.

19. The recombinant vector of claim **17**, wherein the double-stranded RNA molecule comprises a 3' cholesterol conjugation.

20. The recombinant vector of claim **17**, wherein the double-stranded RNA molecule comprises at least one modified nucleoside selected from inosine, 1-methyladenosine, 2-methyladenosine, N^6-methyladenosine, N^6-isopentenyladenosine, 2'-O-methyladenosine, N^6-acetyladenosine, 1-methylinosine, pseudouridine, dihydrouridine, or 2-methylthio-N^6-methyladenosine.

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