[0021] In one embodiment, the collagen is linked to the protein directly or through a linker, wherein the linker is a flexible linker, such as $(G)_a$ or $(GGGGS)_b$ (SEQ ID NO. 4), wherein a and b are each independently an integer from 1 to 10 or from 1 to 5 or from 1 to 3.

[0022] In one embodiment, the medical device or the medicament or the drug-device combination product or the kit is also used for preventing and/or treating an ultraviolet photoaging-induced skin injury or a diabetic infected wound.

[0023] In one embodiment, the medical device is a gel, a dressing, an invasive device, or an implantable device.

[0024] In one embodiment, n is an integer from 1 to 32. In one embodiment, when n is an integer greater than or equal to 2, the repeat sequences are directly linked to each other. In one embodiment, n is 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, or 31.

[0025] In one embodiment, the collagen comprises the sequence set forth in SEQ ID NO. 2 (GPPGPCCGGG) or does not comprise the sequence set forth in SEQ ID NO. 2 (GPPGPCCGGG).

[0026] In one embodiment, the collagen comprises:

[0027] a) an amino acid sequence of SEQ ID NO. 3;

[0028] b) an amino acid sequence having at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identity to the amino acid sequence of SEQ ID NO. 3 while retaining the anti-endothelial cell injury effect of the amino acid sequence of SEQ ID NO. 3; or

[0029] c) an amino acid sequence in which 1 to 80 (such as 1 to 70, 1 to 60, 1 to 50, 1 to 40, 1 to 30, 1 to 10, 1 to 8 or 1 to 5) amino acid residues are added, substituted, deleted or inserted into the amino acid sequence of SEQ ID NO. 3 while retaining the anti-endothelial cell injury effect of the amino acid sequence of SEQ ID NO. 3.

[0030] In one embodiment, the amino acid sequence of SEQ ID NO. 3 is

[0031] GERGAPGFRGPAGPNGIPGEKGPAGERGAPGERGAPGFRGPAGPNGIPGEKGP
AGERGAPGERGAPGFRGPAGPNGIPGEKGPAGERGAPGERGAPGFRGPAGPNGIPGEK
GPAGERGAPGERGAPGFRGPAGPNGIPGEKGPAGERGAPGERGAPGFRGPAGPNGIPG
EKGPAGERGAPGERGAPGFRGPAGPNGIPGEKGPAGERGAPGERGAPGFRGPAGPNGI
PGEKGPAGERGAPGERGAPGFRGPAGPNGIPGEKGPAGERGAPGERGAPGFRGPAGPN
GIPGEKGPAGERGAPGERGAPGFRGPAGPNGIPGEKGPAGERGAPGERGAPGFRGPAG

PNGIPGEKGPAGERGAPGERGAPGFRGPAGPNGIPGEKGPAGERGAPGERGAPGFRGP AGPNGIPGEKGPAGERGAPGERGAPGFRGPAGPNGIPGEKGPAGERGAPGERGAPGFR GPAGPNGIPGEKGPAGERGAP (SEQ ID NO. 3). In the present disclosure, a collagen having the amino acid sequence of SEQ ID NO: 3 is also referred to as RhCOL III.

[0032] In one embodiment, the cardiovascular disease is a cardiovascular disease associated with an endothelial cell injury. In one embodiment, the endothelial cell injury is an endothelial cell injury induced by angiotensin II or ROS, and/or the vascular injury is a vascular injury induced by angiotensin II or ROS. In one embodiment, the vascular injury is a vascular endothelial injury, preferably a diabetic vascular endothelial injury.

[0033] In one embodiment, the cardiovascular disease is selected from arteriosclerosis, atherosclerosis, hypertension, coronary heart disease, peripheral vascular disease, stroke, heart failure, arrhythmia, cerebrovascular disease, atrial fibrillation, and thrombotic disease. In one embodiment, the hypertension is spontaneous hypertension.

[0034] In one embodiment, the medical device or the medicament or the kit is a medical device or a medicament or a kit for lowering blood pressure.

[0035] In one embodiment, the composition comprises a lipid-regulating agent and/or an antihypertensive agent, such as statins, an angiotensin converting enzyme inhibitor, a calcium channel blocker and/or a beta receptor blocker.

[0036] In the second aspect, the present application provides a pharmaceutical composition or a medical device or a drug-device combination product. In one embodiment, the pharmaceutical composition comprises the collagen, the fusion protein comprising the collagen, the nucleic acid encoding the collagen or the fusion protein, the vector comprising the nucleic acid, the host cell comprising the vector in the first aspect hereabove, and an agent for preventing and/or treating a cardiovascular disease or for the repair of a vascular injury. In one embodiment, the agent is a lipid-regulating agent and/or an antihypertensive agent, such as statins, an angiotensin converting enzyme inhibitor, a calcium channel blocker and/or a beta receptor blocker. In another embodiment, the medical device or the drug-device combination product comprises the collagen, the fusion protein comprising the collagen, the nucleic acid encoding the collagen or the fusion protein, the vector comprising the nucleic acid, the host cell comprising the vector in the first aspect hereabove, and a material or device for the repair of a vascular injury. Preferably, the medical device is a gel, a dressing, an invasive device, or an implantable device. In one

purposes. In some embodiments, the collagen or recombinant collagen is directly applied to or introduced into the body of the subject, particularly the site of the vascular injury as a medical device. In some embodiments, the collagen or recombinant collagen is used as a medical device in a variety of therapeutic or prophylactic applications. Such applications can be used to prevent or treat a vascular injury, for example, in a vascular injury involving the skin and other collagen-containing structures and organs. The collagen or recombinant collagen described herein can also be used to provide biocompatible coatings for certain medical devices to promote healing of injuries and disorders in body areas in which such devices are used to treat or prevent cardiovascular disease in a subject.

[0119] The following examples are further provided to illustrate the present disclosure.

[0120] Examples

[0121] Hereinafter, the inventive objects, technical features, and beneficial effects of the present disclosure are further described in detail in conjunction with examples, but the embodiments of the present disclosure are not limited thereto.

[0122] The inventors performed cytotoxicity experiments, which verified that RhCOL III had no effect on the cell viability of human umbilical vein endothelial cells (HUVECs) within the concentration range of 0.1-2 mg/mL.

[0123] The inventors then evaluated the protective effect of RhCOL III on angiotensin II (AngII)-induced endothelial injury in HUVECs. The results showed that RhCOL III inhibited the fluorescence intensity of intracellular reactive oxygen species (ROS).

[0124] RhCOL III used herein was prepared and obtained by the inventors. The sequence was GERGAPGFRGPAGPNGIPGEKGPAGERGAPGERGAPGFRGPAGPNGIPGEKGPAGERG APGERGAPGFRGPAGPNGIPGEKGPAGERGAPGERGAPGFRGPAGPNGIPGEKGPAGE RGAPGERGAPGFRGPAGPNGIPGEKGPAGERGAPGERGAPGFRGPAGPNGIPGEKGPA GERGAPGERGAPGFRGPAGPNGIPGEKGPAGERGAPGERGAPGFRGPAGPNGIPGEKG PAGERGAPGERGAPGFRGPAGPNGIPGEKGPAGERGAPGERGAPGFRGPAGPNGIPGE KGPAGERGAPGERGAPGFRGPAGPNGIPGEKGPAGERGAPGERGAPGFRGPAGPNGIP GEKGPAGERGAPGERGAPGFRGPAGPNGIPGEKGPAGERGAPGERGAPGFRGPAGPN GIPGEKGPAGERGAPGERGAPGFRGPAGPNGIPGEKGPAGERGAPGERGAPGFRGPAG PNGIPGEKGPAGERGAP (SEQ ID NO. 3). The specific preparation process can be found in CN 201811438582.6.

could significantly alleviate Ang II-induced microtubule injury.

[0142] Example 5: Monitoring blood pressure, heart rate, and body weight in spontaneously hypertensive rats

[0143] Male spontaneously hypertensive rats (SHRs, 8 weeks old) were purchased from Beijing Vital River Laboratory Animal Technology Co., Ltd. (Beijing, China). SHRs were randomly divided into SHR group, captopril treatment group (10 mg/kg/day), and RhCOL III treatment group (10 mg/kg/day), with 6 rats per group. All animals were maintained on a 12-h light-dark cycle (12 h light/12 h dark) under specific pathogen-free (SPF) conditions with a particular constant temperature (20 - 26 °C) and relative humidity (40-70%). The blood pressure of rats in each group was measured using a non-invasive tail artery sphygmomanometer once weekly for 4 consecutive weeks. First, the non-invasive tail artery sphygmomanometer was preheated and calibrated for performance. Then, each rat was placed in a quiet environment to acclimatize to the surroundings. The base of the tail was positioned on the sensor of the sphygmomanometer, aligned with the tail artery, and the measurement button was pressed. The instrument automatically measured the systolic blood pressure, heart rate, and body weight of the rats.

[0144] Experimental results:

[0145] To evaluate the antihypertensive effect of RhCOL III on SHRs, we measured the tail artery blood pressure of SHRs. As shown in Fig. 5, RhCOL III treatment may significantly alleviate the elevated blood pressure. We also evaluated the effects of RhCOL III on body weight, heart rate, and heart weight ratio of SHRs, and the results showed that RhCOL III had no effect on body weight, heart rate, and heart weight ratio. Compared with the control group (SHR group), the RhCOL III treatment group and the captopril treatment group had reduced systolic blood pressure. These results revealed that RhCOL III could reduce blood pressure in spontaneously hypertensive rats.

[0146] Example 6: Biochemical determination of blood samples from spontaneously hypertensive rats

[0147] For each treatment group of Example 5, orbital blood sampling was performed after 4 weeks of continuous injection. The whole blood samples were allowed to stand overnight at 4 °C, then centrifuged at 3000 rpm for 15 min (2-8 °C). The supernatant was collected for immediate analysis, and the content of each indicator was determined according to the

CLAIMS

1. Use of a collagen, a fusion protein comprising the collagen, a nucleic acid encoding the collagen or the fusion protein, a vector comprising the nucleic acid, a host cell comprising the vector, or a composition comprising the collagen, the fusion protein, the nucleic acid, the vector and/or the host cell in the manufacture of a medical device or a medicament or a drug-device combination product or a kit for preventing and/or treating a cardiovascular disease, for repairing a vascular injury, or for preventing and/or treating a vascular injury in a subject, wherein the cardiovascular disease is associated with a vascular endothelial cell injury induced by angiotensin II or ROS, and the vascular injury is a vascular endothelial injury induced by angiotensin II or ROS, wherein the collagen comprises n repeat units and wherein the repeat unit comprises:

(1) an amino acid sequence set forth in SEQ ID NO. 1;

(2) an amino acid sequence having at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identity to the amino acid sequence set forth in SEQ ID NO. 1; or

(3) an amino acid sequence in which a substitution, an addition, a deletion and/or an insertion of 1 to 5 amino acid residues is introduced to the amino acid sequence set forth in SEQ ID NO. 1;

wherein n is an integer greater than or equal to 1, wherein when n is an integer greater than or equal to 2, the repeat sequences are directly linked to each other;

wherein the collagen comprises the amino acid sequence set forth in SEQ ID NO. 2 at its C- or N- terminus or does not comprise the amino acid sequence set forth in SEQ ID NO. 2; and

wherein the collagen has an anti-endothelial cell injury effect.

2. The use according to claim 1, wherein n is 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, or 32.

3. The use according to claim 1 or 2, wherein one or more of the following applies:

(1) the subject has an ultraviolet photoaging-induced skin injury or a diabetic infected wound;

(2) the medical device or the medicament or the drug-device combination product or the kit is further capable of preventing and/or treating the ultraviolet photoaging-induced skin injury or the diabetic infected wound;

(3) the collagen is a recombinant type III humanized collagen in a trimeric form;

(4) the medical device is a gel, a dressing, an invasive device, or an implantable device.

4. The use according to any one of claims 1-3, wherein the fusion protein comprises the collagen and a protein for promoting secretion, isolation and/or purification of the collagen;and the collagen is linked to the protein directly or through a linker, wherein the linker is a flexible linker, optionally $(G)_a$ or $(GGGGS)_b$ (SEQ ID NO. 4), wherein a and b are each independently an integer from 1 to 10 or from 1 to 5 or from 1 to 3;

optionally, the protein is selected from an enzyme cleavage site sequence, a signal peptide and a purification tag sequence;

optionally, the enzyme cleavage site sequence is a TEV protease cleavage site sequence or the purification tag sequence is His tag, GST tag, MBP tag, SUMO tag, Cytiva Protein Select tag or NusA tag.

5. The use according to any one of claims 1-4, wherein the collagen comprises:

a) an amino acid sequence of SEQ ID NO. 3;

b) an amino acid sequence which has at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identity to the amino acid sequence of SEQ ID NO. 3 while retaining the anti-endothelial cell injury effect of the amino acid sequence of SEQ ID NO. 3; or

c) an amino acid sequence in which 1 to 80, 1 to 70, 1 to 60, 1 to 50, 1 to 40, 1 to 30, 1 to 10, 1 to 8 or 1 to 5 amino acid residues are added, substituted, deleted or inserted into the amino acid sequence of SEQ ID NO. 3 while retaining the anti-endothelial cell injury effect of the amino acid sequence of SEQ ID NO. 3.

6. The use according to any one of claims 1-5, wherein the the medical device or medicament or drug-device combination product is intended for administration via an oral or parenteral route, or via intravenous, intramuscular, intraarterial, intrathecal, intracapsular, intraorbital, intracardiac, intradermal, intraperitoneal, intratracheal, subcutaneous, subepidermal, intraarticular, subcapsular, subarachnoid, intraspinal, epidural, or intrasternal injection or infusion.

7. The use according to any one of claims 1-6, wherein the cardiovascular disease is selected from arteriosclerosis, atherosclerosis, hypertension, coronary heart disease, peripheral vascular disease, stroke, heart failure, arrhythmia, cerebrovascular disease, atrial fibrillation, and

thrombotic disease; optionally, wherein the hypertension is spontaneous hypertension; the vascular endothelial injury is diabetic vascular endothelial injury.

8. The use according to any one of claims 1-7, wherein the composition comprises a lipid-regulating agent and/or an antihypertensive agent, optionally statins, an angiotensin converting enzyme inhibitor, a calcium channel blocker and/or a beta receptor blocker.

9. A pharmaceutical composition comprising the collagen, the fusion protein comprising the collagen, the nucleic acid encoding the collagen or the fusion protein, the vector comprising the nucleic acid, the host cell comprising the vector in any one of claims 1 to 5, and an agent for preventing and/or treating a cardiovascular disease or for the repair of a vascular injury, wherein the cardiovascular disease is associated with a vascular endothelial cell injury induced by angiotensin II or ROS, and the vascular injury is a vascular endothelial injury induced by angiotensin II or ROS, wherein the agent is optionally a lipid-regulating agent and/or an antihypertensive agent, optionally statins, an angiotensin converting enzyme inhibitor, a calcium channel blocker and/or a beta receptor blocker.

10. A medical device comprising the collagen, the fusion protein comprising the collagen, the nucleic acid encoding the collagen or the fusion protein, the vector comprising the nucleic acid, the host cell comprising the vector in any one of claims 1-5, and a material or device for the repair of a vascular injury; wherein the vascular injury is a vascular endothelial injury induced by angiotensin II or ROS, wherein optionally the medical device is a gel, a dressing, an invasive device, or an implantable device.

11. A method of blocking or eliminating an angiotensin II or ROS-induced vascular endothelial cell injury *in vitro*, comprising a step of contacting a vascular endothelial cell with the collagen in any one of claims 1 to 5, wherein optionally, the vascular endothelial cell is an umbilical vein vascular endothelial cell or a human umbilical vein vascular endothelial cell.

12. An *in vitro* method for (1) reducing angiotensin II-induced ROS production in a cell or (2) alleviating Ang II-induced microtubule injury in a cell, comprising a step of contacting the cell with the collagen in any one of claims 1 to 5, wherein the cell is a vascular endothelial cell or an umbilical vein vascular endothelial cell or a human umbilical vein vascular endothelial cell.

13. A method of screening for an active ingredient for preventing and/or treating a cardiovascular disease or for the repair of a vascular injury in a subject, comprising

(i) providing a collagen comprising n repeat units, wherein the repeating unit comprises:

(1) a sequence set forth in SEQ ID NO. 1;

(2) a sequence having at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identity to the sequence set forth in SEQ ID NO. 1; or

(3) a sequence in which a substitution, an addition, a deletion and/or an insertion of 1 to 5 amino acid residues is introduced to the sequence set forth in SEQ ID NO. 1;

wherein n is an integer greater than or equal to 1, optionally an integer ranging from 1 to 32, optionally 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30 or 31, wherein when n is an integer greater than or equal to 2, the repeat sequences are directly linked to each other;

(ii) adding the collagen to an angiotensin II-treated HUVEC cell;

(iii) selecting a collagen having a property of: (a) reducing ROS generation/or (b) alleviating a microtubule injury, as an active ingredient;

wherein the cardiovascular disease is associated with an endothelial cell injury induced by angiotensin II or ROS, and the vascular injury is a vascular endothelial injury induced by angiotensin II or ROS.

14. The method according to claim 13, wherein one or more of the following applies:

(1) the subject has an ultraviolet photoaging-induced skin injury or a diabetic infected wound;

(2) the collagen has an anti-endothelial cell injury effect;

(3) the active ingredient is further capable of preventing and/or treating the ultraviolet photoaging-induced skin injury or the diabetic infected wound;

(4) wherein the cardiovascular disease is selected from atherosclerosis, hypertension, coronary heart disease, peripheral vascular disease, stroke, heart failure, arrhythmia, cerebrovascular disease, atrial fibrillation, and thrombotic disease;

(5) the active ingredient is useful as a medicament or as a medical device or as a drug-device combination product.

15. The method according to claim 13 or 14, wherein the selected collagen comprises:

a) the amino acid sequence of SEQ ID NO. 3;

b) an amino acid sequence having at least 80%, at least 85%, at least 90%, at least 91%, at

least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identity to the amino acid sequence set forth in SEQ ID NO. 3; or

c) an amino acid sequence in which 1 to 80, 1 to 70, 1 to 60, 1 to 50, 1 to 40, 1 to 30, 1 to 10, 1 to 8 or 1 to 5 amino acid residues are added, substituted, deleted or inserted into the amino acid sequence of SEQ ID NO. 3.