

METHODS AND COMPOSITIONS FOR PREVENTING AND TREATING ATHEROSCLEROSIS AND RELATED DISEASES

TECHNICAL FIELD

The content of the present invention belongs to the field of biomedicines, and relates to methods and compositions for preventing and treating atherosclerosis and related diseases.

BACKGROUND

Atherosclerosis refers to the dysfunction of arterial vessels due to lipid accumulation in arterial vessel walls forming lipid streaks or atherosclerotic plaques. Arterial vasomotor function decrease, luminal stenosis and even thrombus due to plaque formation in turn affect the blood supply of tissues and organs supplied by the artery, resulting in local or overall ischemia of the tissues and organs.

For a long time, there has been a demand for drugs and/or treatment methods that can more effectively prevent and/or treat atherosclerosis and atherosclerosis-related diseases.

SUMMARY

Therefore, there is a need for novel treatment methods for atherosclerosis or atherosclerosis-related diseases. The present invention fulfills such need and also provides related advantages. The method, composition and/or application of the present disclosure can significantly reduce the level of oxidized low-density lipoprotein in disease model animals, reduce atherosclerotic plaque formation, and inhibit the progression of atherosclerosis.

In one aspect, provided herein is a use of a therapeutically effective amount of sDSS1 protein or a fragment or variant thereof, a nucleic acid encoding said sDSS1 protein or a fragment or variant thereof or a vector containing said nucleic acid, transplanting into said individual with a cell expressing said sDSS1 protein or a fragment or variant thereof, or tissues or organs containing said sDSS1 protein or a fragment or variant thereof or said nucleic acid, and/or infusing into the individual serum or interstitial fluid containing said sDSS1 protein or a fragment or variant thereof or said nucleic acid in the manufacture of a medicament for preventing or treating atherosclerosis or atherosclerosis-related diseases in an individual in need thereof, wherein the medicament is to be administered to said individual.

In one aspect, provided herein is a use of a therapeutically effective amount of sDSS1 protein or a fragment or variant thereof in the manufacture of a medicament for reducing lipid absorption by vascular endothelium in an individual in need thereof.

In one aspect, provided herein is a use of a therapeutically effective amount of sDSS1 protein or a fragment or variant thereof in the manufacture of a medicament for reducing lipid accumulation in macrophages in an individual in need thereof.

In one aspect, provided herein is a use of a therapeutically effective amount of sDSS1 protein or a fragment or variant thereof in the manufacture of a medicament for increasing lipid accumulation in liver cells in an individual in need thereof.

In one aspect, provided herein is a use of an effective amount of sDSS1 protein or a fragment or variant thereof, wherein the sDSS1 protein or a fragment or variant thereof can form a complex with free oxidized LDL in the manufacture of a medicament for reducing the amount of circulating oxidized LDL in the blood vessels of an individual.

In one aspect, provided herein is a use of an effective amount of sDSS1 protein or a fragment or variant thereof, wherein the sDSS1 protein or a fragment or variant thereof can form a complex with free oxidized LDL in the manufacture of a medicament for reducing plaque formation in the blood vessels of an individual.

In one example, provided herein is a method for preventing or treating atherosclerosis or atherosclerosis-related diseases in an individual in need thereof, comprising administering to the individual a therapeutically effective amount of sDSS1 protein or a fragment or variant thereof, a nucleic acid encoding the sDSS1 protein or a fragment or variant thereof or a vector containing the nucleic acid, transplanting into the individual with a cell expressing the sDSS1 protein or a fragment or variant thereof, or tissues or organs containing the sDSS1 protein or a fragment or variant thereof or the nucleic acid, and/or infusing into the individual serum or interstitial fluid containing the sDSS1 protein or a fragment or variant thereof or the nucleic acid.

In some specific examples, the sDSS1 protein or a fragment or variant thereof has at least 80%, 85%, 90%, 95%, 98%, or 100% sequence identity with the sequence as shown in SEQ ID NO:1. In some specific examples, the sDSS1 protein or a fragment or variant thereof comprises insertion, deletion or substitution of no more than 10, 9, 8, 7, 6, 5, 4, 3, 2 or 1 amino acid(s) compared with the sequence as shown in SEQ ID NO: 1. In some specific examples, the sDSS1 protein or a fragment or variant thereof comprises non-natural amino acids. In some specific examples, the non-natural amino acids comprise hydroxyproline, hydroxylysine, selenocysteine, D-amino acids, or synthetic non-natural amino acids and derivatives thereof. In some specific

examples, the sDSS1 protein or a fragment or variant thereof comprises an amino acid sequence as shown in SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO: 10, SEQ ID NO: 11, SEQ ID NO: 12, SEQ ID NO: 13, or SEQ ID NO: 14. In some specific examples, the sDSS1 protein or a fragment or variant thereof comprises a fragment having at least 80%, 85%, 90%, 95%, 98%, or 100% sequence identity with the sequence as shown in SEQ ID NO: 17 and a fragment having at least 80%, 85%, 90%, 95%, 98%, or 100% sequence identity with the sequence as shown in SEQ ID NO: 18.

In some specific examples, the sDSS1 protein or a fragment or variant thereof comprises a fragment having at least 80%, 85%, 90%, 95%, 98%, or 100% sequence identity with the sequence as shown in SEQ ID NO: 17 and a fragment that contributes to achieving transmembrane transport function. In some specific examples, the sDSS1 protein or a fragment or variant thereof comprises chemical modifications on 1 to 20 amino acids. In some specific examples, the chemical modification comprises amino or glycosylation modification, fatty acid modification, acylation modification, Fc fragment fusion, albumin fusion, pegylation modification, dextran modification, heparin modification, polyvinylpyrrolidone modification, polyamino acid modification, polysialic acid modification, chitosan and its derivative modification, lectin modification, sodium alginate modification, carbomer modification, polyvinylpyrrolidone modification, hydroxypropyl methylcellulose modification, hydroxypropyl cellulose modification, acetylation modification, formylation modification, phosphorylation modification, methylation modification and/or sulfonation modification. In some specific examples, the vector comprises a eukaryotic expression plasmid vector, adenovirus, adeno-associated virus, lentivirus, retrovirus, baculovirus, herpes virus, or pseudorabies virus. In some specific examples, the cell is any one of a stem cell, a precursor cell or an adult cell of humans. In some specific examples, the stem cell is an induced pluripotent stem cell, a cell obtained by transdifferentiation, or a stem cell derived from a primary culture, a pluripotent or unipotent stem cell differentiated from a parent cell. In some specific examples, the tissue is a whole organ or a partial tissue mass of a brain, liver, kidney, spleen or pancreatic islets, or blood, fat, muscle, bone marrow or skin. In some specific examples, the method further comprises administering a hypolipidemic drug to the individual. In some specific examples, the method further comprises administering an antihypertensive drug to the individual. In some specific examples, the method further comprises administering an anticoagulant to the individual. In some specific examples, the individual undergoes a surgical procedure selected from a group consisting of percutaneous

coronary intervention, coronary artery bypass grafting, or carotid endarterectomy. In some specific examples, the method reduces lipid accumulation in the arterial vessel walls. In some specific examples, the lipid comprises one or more of cholesterol, cholesterol ester, triglyceride, chylomicron (CM), low-density lipoprotein (LDL), very low-density lipoprotein (VLDL), intermediate density lipoprotein (IDL), lipoprotein (a) (Lp(a)), oxidized low-density lipoprotein (oxLDL) and the respective metabolic intermediates thereof in the blood. In some specific examples, the atherosclerosis or atherosclerosis-related diseases comprise vascular inner diameter stenosis, vascular outer diameter dilation, decreased vasoconstriction and vasodilatation capacity, decreased vascular elasticity, increased vascular fragility, angiolithic degeneration or calcinosis, or thrombus-induced reduction in blood supply capacity of blood vessels. In some specific examples, the atherosclerosis or atherosclerosis-related diseases comprise hypertension, angina pectoris, myocardial infarction, myocardium blood-supply insufficiency, arrhythmia, cerebral blood supply insufficiency, cerebral ischemic stroke, cerebral atrophy, renal insufficiency, renal artery stenosis, paralytic ileus, or acral ischemic necrosis.

In another example, provided herein is a method for reducing lipid absorption by vascular endothelium in an individual in need thereof, comprising administering to the individual a therapeutically effective amount of sDSS1 protein or a fragment or variant thereof. In some specific examples, the sDSS1 protein or a fragment or variant thereof has at least 80%, 85%, 90%, 95%, 98%, or 100% sequence identity with the sequence as shown in SEQ ID NO: 1. In some specific examples, the sDSS1 protein or a fragment or variant thereof comprises insertion, deletion or substitution of no more than 10, 9, 8, 7, 6, 5, 4, 3, 2 or 1 amino acid(s) compared with the sequence as shown in SEQ ID NO: 1. In some specific examples, the sDSS1 protein or a fragment or variant thereof comprises non-natural amino acids. In some specific examples, the non-natural amino acids comprise hydroxyproline, hydroxylysine, selenocysteine, D-amino acids, or synthetic non-natural amino acids and derivatives thereof. In some specific examples, the sDSS1 protein or a fragment or variant thereof comprises an amino acid sequence as shown in SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO: 10, SEQ ID NO: 11, SEQ ID NO: 12, SEQ ID NO: 13, or SEQ ID NO: 14. In some specific examples, the sDSS1 protein or a fragment or variant thereof comprises a fragment having at least 80%, 85%, 90%, 95%, 98%, or 100% sequence identity with the sequence as shown in SEQ ID NO: 17 and a fragment having at least 80%, 85%, 90%, 95%, 98%, or 100% sequence identity with the sequence as shown in SEQ ID NO: 18.

In another example, provided herein is a method for reducing lipid accumulation in macrophages in an individual in need thereof, comprising administering to the individual a therapeutically effective amount of sDSS1 protein or a fragment or variant thereof. In some specific examples, the sDSS1 protein or a fragment or variant thereof has at least 80%, 85%, 90%, 95%, 98%, or 100% sequence identity with the sequence as shown in SEQ ID NO:1. In some specific examples, the sDSS1 protein or a fragment or variant thereof comprises insertion, deletion or substitution of no more than 10, 9, 8, 7, 6, 5, 4, 3, 2 or 1 amino acid(s) compared with the sequence as shown in SEQ ID NO: 1. In some specific examples, the sDSS1 protein or a fragment or variant thereof comprises non-natural amino acids. In some specific examples, the non-natural amino acids comprise hydroxyproline, hydroxylysine, selenocysteine, D-amino acids, or synthetic non-natural amino acids and derivatives thereof. In some specific examples, the sDSS1 protein or a fragment or variant thereof comprises an amino acid sequence as shown in SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO: 10, SEQ ID NO: 11, SEQ ID NO: 12, SEQ ID NO: 13, or SEQ ID NO: 14. In some specific examples, the sDSS1 protein or a fragment or variant thereof comprises a fragment having at least 80%, 85%, 90%, 95%, 98%, or 100% sequence identity with the sequence as shown in SEQ ID NO: 17 and a fragment having at least 80%, 85%, 90%, 95%, 98%, or 100% sequence identity with the sequence as shown in SEQ ID NO: 18.

In another example, provided herein is a method for increasing lipid accumulation in liver cells in an individual in need thereof, comprising administering to the individual a therapeutically effective amount of sDSS1 protein or a fragment or variant thereof. In some specific examples, the sDSS1 protein or a fragment or variant thereof has at least 80%, 85%, 90%, 95%, 98%, or 100% sequence identity with the sequence as shown in SEQ ID NO: 1. In some specific examples, the sDSS1 protein or a fragment or variant thereof comprises insertion, deletion or substitution of no more than 10, 9, 8, 7, 6, 5, 4, 3, 2 or 1 amino acid(s) compared with the sequence as shown in SEQ ID NO: 1. In some specific examples, the sDSS1 protein or a fragment or variant thereof comprises non-natural amino acids. In some specific examples, the non-natural amino acids comprise hydroxyproline, hydroxylysine, selenocysteine, D-amino acids, or synthetic non-natural amino acids and derivatives thereof. In some specific examples, the sDSS1 protein or a fragment or variant thereof comprises an amino acid sequence as shown in SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO: 10, SEQ ID NO: 11, SEQ ID

NO: 12, SEQ ID NO: 13, or SEQ ID NO: 14. In some specific examples, the sDSS1 protein or a fragment or variant thereof comprises a fragment having at least 80%, 85%, 90%, 95%, 98%, or 100% sequence identity with the sequence as shown in SEQ ID NO: 17 and a fragment having at least 80%, 85%, 90%, 95%, 98%, or 100% sequence identity with the sequence as shown in SEQ ID NO: 18.

In another example, provided herein is a method for reducing the amount of circulating oxidized LDL in the blood vessels of an individual, comprising administering to the individual an effective amount of sDSS1 protein or a fragment or variant thereof, wherein the sDSS1 protein or a fragment or variant thereof can form a complex with free oxidized LDL. In some examples, the method reduces the amount of free uncomplexed oxidized LDL and the amount of total oxidized LDL. In some specific examples, the sDSS1 protein or a fragment or variant thereof has at least 80%, 85%, 90%, 95%, 98%, or 100% sequence identity with the sequence as shown in SEQ ID NO: 1. In some specific examples, the sDSS1 protein or a fragment or variant thereof comprises insertion, deletion or substitution of no more than 10, 9, 8, 7, 6, 5, 4, 3, 2 or 1 amino acid(s) compared with the sequence as shown in SEQ ID NO: 1. In some specific examples, the sDSS1 protein or a fragment or variant thereof comprises non-natural amino acids. In some specific examples, the non-natural amino acids comprise hydroxyproline, hydroxylysine, selenocysteine, D-amino acids, or synthetic non-natural amino acids and derivatives thereof. In some specific examples, the sDSS1 protein or a fragment or variant thereof comprises an amino acid sequence as shown in SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO: 10, SEQ ID NO: 11, SEQ ID NO: 12, SEQ ID NO: 13, or SEQ ID NO: 14. In some specific examples, the sDSS1 protein or a fragment or variant thereof comprises a fragment having at least 80%, 85%, 90%, 95%, 98%, or 100% sequence identity with the sequence as shown in SEQ ID NO: 17 and a fragment having at least 80%, 85%, 90%, 95%, 98%, or 100% sequence identity with the sequence as shown in SEQ ID NO: 18.

In another example, provided herein is a method for reducing plaque formation in the blood vessels of an individual, comprising administering to the individual an effective amount of sDSS1 protein or a fragment or variant thereof, wherein the sDSS1 protein or a fragment or variant thereof can form a complex with free oxidized LDL. In some specific examples, the blood vessel is an artery. In some specific examples, the blood vessel is an aorta. In some specific examples, the sDSS1 protein or a fragment or variant thereof has at least 80%, 85%, 90%, 95%, 98%, or 100% sequence identity with the sequence as shown in SEQ ID NO: 1. In some specific

examples, the sDSS1 protein or a fragment or variant thereof comprises insertion, deletion or substitution of no more than 10, 9, 8, 7, 6, 5, 4, 3, 2 or 1 amino acid(s) compared with the sequence as shown in SEQ ID NO: 1. In some specific examples, the sDSS1 protein or a fragment or variant thereof comprises non-natural amino acids. In some specific examples, the non-natural amino acids comprise hydroxyproline, hydroxylysine, selenocysteine, D-amino acids, or synthetic non-natural amino acids and derivatives thereof. In some specific examples, the sDSS1 protein or a fragment or variant thereof comprises an amino acid sequence as shown in SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO: 10, SEQ ID NO: 11, SEQ ID NO: 12, SEQ ID NO: 13, or SEQ ID NO: 14. In some specific examples, the sDSS1 protein or a fragment or variant thereof comprises a fragment having at least 80%, 85%, 90%, 95%, 98%, or 100% sequence identity with the sequence as shown in SEQ ID NO: 17 and a fragment having at least 80%, 85%, 90%, 95%, 98%, or 100% sequence identity with the sequence as shown in SEQ ID NO: 18.

In another example, provided herein is a method for sequestering circulating free oxidized LDL in blood vessels in the form of a protein-lipid complex, comprising exposing the oxidized LDL to the protein to form the protein-lipid complex in the blood vessels, wherein the protein is sDSS1 protein or a fragment or variant thereof. In some specific examples, the sDSS1 protein or a fragment or variant thereof has at least 80%, 85%, 90%, 95%, 98%, or 100% sequence identity with the sequence as shown in SEQ ID NO: 1. In some specific examples, the sDSS1 protein or a fragment or variant thereof comprises insertion, deletion or substitution of no more than 10, 9, 8, 7, 6, 5, 4, 3, 2 or 1 amino acid(s) compared with the sequence as shown in SEQ ID NO: 1. In some specific examples, the sDSS1 protein or a fragment or variant thereof comprises non-natural amino acids. In some specific examples, the non-natural amino acids comprise hydroxyproline, hydroxylysine, selenocysteine, D-amino acids, or synthetic non-natural amino acids and a derivative thereof. In some specific examples, the sDSS1 protein or a fragment or variant thereof comprises an amino acid sequence as shown in SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO: 10, SEQ ID NO: 11, SEQ ID NO: 12, SEQ ID NO: 13, or SEQ ID NO: 14. In some specific examples, the sDSS1 protein or a fragment or variant thereof comprises a fragment having at least 80%, 85%, 90%, 95%, 98%, or 100% sequence identity with the sequence as shown in SEQ ID NO: 17 and a fragment having at least 80%, 85%, 90%, 95%, 98%, or 100% sequence identity with the sequence as shown in SEQ ID NO: 18.

In another example, provided herein is a complex of sDSS1 protein or a fragment or variant thereof and lipids.

In another example, provided herein is a method for screening a therapeutic agent for the treatment of atherosclerosis or atherosclerosis-related diseases in an individual in need thereof, comprising contacting the therapeutic agent with sDSS1 protein, the gene of the sDSS1 protein, the regulatory elements of the sDSS1 gene and the transcription product of the sDSS1 gene, and evaluating the effect of the therapeutic agent on the expression of the sDSS1 protein.

For example, the following technical solutions are provided herein:

an application of a protein in the preparation of drugs for the prevention and treatment of atherosclerosis or atherosclerosis-related cardiovascular and cerebrovascular diseases and peripheral vascular diseases, characterized in that the application is to use sDSS1 protein for the preparation of drugs for the prevention and treatment of atherosclerosis or atherosclerosis-related cardiovascular and cerebrovascular diseases and peripheral vascular diseases.

In some specific examples, the atherosclerosis refers to the appearance of lipid streaks or atherosclerotic plaques caused by lipid accumulation in arterial vessel walls, leading to dysfunction of arterial vessels.

In some specific examples, the lipid refers to one or more of cholesterol, cholesterol ester, triglyceride, chylomicron (CM), low-density lipoprotein (LDL), very low-density lipoprotein (VLDL), intermediate density lipoprotein (IDL), lipoprotein (a) (Lp(a)), high density lipoprotein (HDL), oxidized low-density lipoprotein (oxLDL) and the respective metabolic intermediate thereof in the blood.

In some specific examples, the dysfunction of arterial vessels refers to vascular inner diameter stenosis, vascular outer diameter dilation, decreased vasoconstriction and vasodilatation capacity, decreased vascular elasticity, increased vascular fragility, angiolithic degeneration or calcinosis, and thrombus-induced reduction in blood supply capacity of blood vessels.

In some specific examples, the atherosclerosis-related cardiovascular diseases refer to hypertension, angina pectoris, myocardial infarction, myocardium blood-supply insufficiency, arrhythmia, and sudden death.

In some specific examples, the atherosclerotic-related cerebrovascular diseases refer to cerebral blood supply insufficiency, cerebral ischemic stroke, and cerebral atrophy.

In some specific examples, the atherosclerosis-related peripheral vascular diseases refer to renal insufficiency, renal artery stenosis, paralytic ileus, or acral ischemic necrosis.

In some specific examples, the sDSS1 protein comprises a basic protein formed by sDSS1 protein sequence of any one of Homo sapiens, Pan troglodytes, Pan paniscus, Gorilla, Orangutan, Nomascus leucogenys, Rhinopithecus roxellana, Macaca mulatta, Rhinopithecus bieti, Papio anubis, Colobus angolensis, Cercopithecus atys, Mandrillus leucophaeus, and Macaca leonina, wherein the amino acid sequence of Homo sapiens sDSS1 is set forth as SEQ ID NO:1, the amino acid sequence of Pan troglodytes sDSS1 is set forth as SEQ ID NO: 2, the amino acid sequence of Pan paniscus sDSS1 is set forth as SEQ ID NO: 3, the amino acid sequence of Gorilla sDSS1 is set forth as SEQ ID NO: 4, the amino acid sequence of Orangutan sDSS1 is set forth as SEQ ID NO: 5, the amino acid sequence of Nomascus leucogenys sDSS1 is set forth as SEQ ID NO: 6, the amino acid sequence of Rhinopithecus roxellana sDSS1 is set forth as SEQ ID NO: 7, the amino acid sequence of Macaca mulatta sDSS1 is set forth as SEQ ID NO: 8, the amino acid sequence of Rhinopithecus bieti sDSS1 is set forth as SEQ ID NO: 9, the amino acid sequence of Papio anubis sDSS1 is set forth as SEQ ID NO: 10, the amino acid sequence of Colobus angolensis sDSS1 is set forth as SEQ ID NO: 11, the amino acid sequence of Cercopithecus atys sDSS1 is set forth as SEQ ID NO: 12, the amino acid sequence of Mandrillus leucophaeus sDSS1 is set forth as SEQ ID NO: 13, and the amino acid sequence of Macaca leonina sDSS1 is set forth as SEQ ID NO: 14.

In some specific examples, the sDSS1 protein is any first protein having more than 70% similarity to the sDSS1 protein as described in the aforementioned examples.

In some specific examples, the sDSS1 protein is any second protein based on the 58 amino acids at the N-terminus of the sDSS1 protein as described in the aforementioned examples, fused to other polypeptide fragments at the N-terminus or C-terminus, with the structural characteristics or amino acid sequence characteristics of the polypeptide fragments used for fusion the same as or similar to the 31 amino acids at the C-terminus of the sDSS1 protein as described in the aforementioned examples.

In some specific examples, the sDSS1 protein is any third protein based on the 58 amino acids at the N-terminus of the sDSS1 protein as described in the aforementioned examples, fused to other amino acid fragments at the N-terminus or C-terminus, with the fused protein enabling the transmembrane transport function.

In some specific examples, the sDSS1 protein is a fusion protein formed by ligation of the basic protein, the first protein, the second protein, or the third protein to the protein itself, carrier protein, antibody or other amino acid fragments of any length.

In some specific examples, the sDSS1 protein is a polypeptide/protein modifier produced by the modification based on the basic protein, the first protein, the second protein, the third protein, or the fusion protein.

In some specific examples, the polypeptide/protein modifier is chemically modified for amino groups on amino acid side chains, carbonyl groups on amino acid side chains, nitrogen-terminal amino groups, carbon-terminal carbonyl groups, cysteine, tyrosine, serine and tryptophan at 1-20 sites either specifically or non-specifically.

In some specific examples, the modification method of the polypeptide/protein modifier comprises one or more than one of glycosylation modification, fatty acid modification, acylation modification, Fc fragment fusion, albumin fusion, pegylation modification, dextran modification, heparin modification, polyvinylpyrrolidone modification, polyamino acid modification, polysialic acid modification, chitosan and its derivative modification, lectin modification, sodium alginate modification, carbomer modification, polyvinylpyrrolidone modification, hydroxypropyl methylcellulose modification, hydroxypropyl cellulose modification, acetylation modification, formylation modification, phosphorylation modification, methylation modification, sulfonation modification, and other pharmaceutically available polypeptide/protein modification modification methods.

In some specific examples, the sDSS1 protein is a non-natural amino acid substitute protein with substitutions performed at 1 to 31 arbitrary amino acid sites using amino acids other than the 20 basic amino acids based on the amino acid sequence of the basic protein, the first protein, the second protein, the third protein, or the fusion protein.

In some specific examples, the amino acid substitutions of the non-natural amino acid substitute protein comprise hydroxyproline, hydroxylysine, selenocysteine, D-amino acids, synthetic non-natural amino acids and derivatives thereof.

In some specific examples, the sDSS1 protein is a partial or full complex formed by the basic protein, the first protein, the second protein, the third protein, the fusion protein, the polypeptide/protein modifier or the non-natural amino acid substitute and a pharmaceutically applicable drug carrier.

In some specific examples, the drug carrier of the complex comprises one or more than one of an enteric coated formulation, a capsule, a micro-sphere/-capsule, a liposome, a microemulsion, a composite emulsion, a nanoparticle, a magnetic particle, gelatin and gel.

In some specific examples, the sDSS1 protein targets the individual's own sDSS1 protein, and the level of the individual's own sDSS1 protein is affected by an exogenous drug.

In some specific examples, the drug uses the sDSS1 protein, the gene of the sDSS1 protein, the regulatory elements of the sDSS1 gene, and the transcription product of the sDSS1 gene as the targets of the drug.

In some specific examples, the drug regulates the amount of the sDSS1 protein in blood, cerebrospinal fluid or lymphatic fluid by affecting protease/peptidase activity in blood, cerebrospinal fluid or lymphatic fluid.

In some specific examples, the drug is a first drug formed by a chemical small molecular drug, an antibody, a polypeptide/protein drug, a nucleic acid drug, or a nano-drug.

In some specific examples, the sDSS1 protein is a second drug formed by a combination of two or more components of any one of the basic protein, the first protein, the second protein, the third protein, the fusion protein, the polypeptide/protein modifier, the complex, and the first drug.

In some specific examples, the sDSS1 protein is a third drug formed by one, two or more components of any one of the basic protein, the first protein, the second protein, the third protein, the fusion protein, the polypeptide/protein modifier, the complex, and the first drug with a pharmaceutically available excipient.

In some specific examples, the sDSS1 protein is a fourth drug obtained by introducing in vivo and expressing through an expression system the nucleotide sequence encoding the basic protein, the first protein, the second protein, the third protein or the fusion protein.

In some specific examples, the expression system is a eukaryotic expression plasmid vector, adenovirus, adeno-associated virus, lentivirus, retrovirus, baculovirus, herpes virus, pseudorabies virus, ZFN gene editing technology, TALEN Gene editing technology, CRISPR/Cas gene editing technology and other medically available gene editing technologies or viral vectors.

In some specific examples, the sDSS1 protein is a fifth protein formed by the basic protein, the first protein, the second protein, the third protein, or the fusion protein obtained by transplanting cells in the individual.

In some specific examples, the cell is any one of a stem cell, a precursor cell or an adult cell of humans.

In some specific examples, the stem cell is an embryonic stem cell, an induced pluripotent stem cell, a cell obtained by transdifferentiation, or a stem cell derived from a primary culture, a pluripotent or unipotent stem cell differentiated from a parent cell.

In some specific examples, the sDSS1 protein is a sixth protein introduced into the individual by infusion of serum, cerebrospinal fluid, lymphatic fluid or interstitial fluid.

In some specific examples, the sDSS1 protein is a seventh protein formed by the basic protein, the first protein, the second protein, the third protein, or the fusion protein obtained by transplanting tissues or organs in the individual.

In some specific examples, the tissue is a whole organ or a partial tissue mass of a brain, liver, kidney, spleen or pancreatic islets, or blood, fat, muscle, bone marrow or skin.

In some specific examples, the preventive drug is one or more of protein drugs, polypeptide drugs, nucleic acid drugs, chemical small molecular drugs, cell products, commercial transplantation tissues, injections, freeze-dried powder, health care products, and food additives comprising the basic protein, any one of the first to the seventh proteins, the fusion protein, the polypeptide/protein modifier, the non-natural amino acid substitute protein, the complex, drug combination, expression system, cell, tissue, organ, body fluid or interstitial fluid.

In some specific examples, the therapeutic drug is one or more of protein drugs, polypeptide drugs, nucleic acid drugs, chemical small molecular drugs, cell products, commercial transplantation tissues, injections, freeze-dried powder, health care products, and food additives comprising the basic protein, any one of the first to the seventh proteins, the fusion protein, the polypeptide/protein modifier, the non-natural amino acid substitute protein, the complex, the first drug, the second drug, the third drug, expression system, cell, tissue, organ, body fluid or interstitial fluid.

The features and/or beneficial effects of the present disclosure include:

1. The sDSS1 protein provided by the present disclosure has the ability to bind to oxLDL and LDL in vitro;
2. The sDSS1 protein provided by the present disclosure can inhibit the uptake of oxLDL by human umbilical vein endothelial cells (HUVECs);
3. The sDSS1 protein provided by the present disclosure can inhibit the phagocytosis of oxLDL by macrophages differentiated from monocyte THP-1;
4. The sDSS1 protein provided by the present disclosure can increase the uptake of oxLDL by hepatocyte HepG2;
5. The sDSS1 protein provided by the present disclosure can reduce the level of oxLDL/LDL ratio in model animals;
6. The sDSS1 protein provided by the present disclosure can reduce the area of atherosclerotic plaques in model animals and inhibit the progression of atherosclerosis.
7. The sDSS1 protein provided by the present disclosure is a protein possessed by humans and other primates, it has a relatively small molecular weight, low immunogenicity, and a natural

protein degradation mechanism in vivo. Therefore, the clinical application thereof will not cause obvious immune responses or other side effects, which is safe and reliable.

In summary, the present disclosure provides a sDSS1 protein drug for the prevention and treatment of atherosclerosis and atherosclerosis-related cardiovascular and cerebrovascular diseases and peripheral vascular diseases. As verified by experiments at the molecular, cellular and animal levels, SDSS1 protein can bind to LDL or oxLDL protein to form a complex, the addition of sDSS1 protein to a culture medium reduces the uptake of oxLDL by vascular endothelial cells and mononuclear macrophages, and increases the uptake of oxLDL by hepatocytes. In animal experiments, sDSS1 protein can effectively reduce the level of oxidized low-density lipoprotein in atherosclerosis model mice, reduce the area of atherosclerotic plaques, and inhibit the progression of atherosclerosis. The sDSS1 protein has lower protein immunogenicity and significant pharmaceutical effect, and has the potential for clinical use in the

CLAIMS

WHAT IS CLAIMED IS:

1. Use of a therapeutically effective amount of sDSS1 protein or a fragment or variant thereof, a nucleic acid encoding said sDSS1 protein or a fragment or variant thereof or a vector containing said nucleic acid, transplanting into said individual with a cell expressing said sDSS1 protein or a fragment or variant thereof, or tissues or organs containing said sDSS1 protein or a fragment or variant thereof or said nucleic acid, and/or infusing into the individual serum or interstitial fluid containing said sDSS1 protein or a fragment or variant thereof or said nucleic acid in the manufacture of a medicament for preventing or treating atherosclerosis or atherosclerosis-related diseases in an individual in need thereof, wherein the medicament is to be administered to said individual.
2. The use according to claim 1, wherein said sDSS1 protein or a fragment or variant thereof has at least 80%, 85%, 90%, 95%, 98%, or 100% sequence identity with the sequence as shown in SEQ ID NO:1.
3. The use according to claim 1, wherein said sDSS1 protein or a fragment or variant thereof comprises insertion, deletion or substitution of no more than 10, 9, 8, 7, 6, 5, 4, 3, 2 or 1 amino acid(s) compared with the sequence as shown in SEQ ID NO: 1.
4. The use according to claim 1, wherein said sDSS1 protein or a fragment or variant thereof comprises non-natural amino acids.
5. The use according to claim 4, wherein said non-natural amino acids comprise hydroxyproline, hydroxylysine, selenocysteine, D-amino acids, or synthetic non-natural amino acids and derivatives thereof.
6. The use according to claim 1, wherein said sDSS1 protein or a fragment or variant thereof comprises an amino acid sequence as shown in SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO: 10, SEQ ID NO: 11, SEQ ID NO: 12, SEQ ID NO: 13, or SEQ ID NO: 14.
7. The use according to claim 1, wherein said sDSS1 protein or a fragment or variant thereof comprises a fragment having at least 80%, 85%, 90%, 95%, 98%, or 100% sequence identity with the sequence as shown in SEQ ID NO: 17 and a fragment having at least 80%, 85%, 90%, 95%, 98%, or 100% sequence identity with the sequence as shown in SEQ ID NO: 18.
8. The use according to claim 1, wherein said sDSS1 protein or a fragment or variant thereof comprises a fragment having at least 80%, 85%, 90%, 95%, 98%, or 100% sequence identity with the sequence as shown in SEQ ID NO: 17 and a fragment that contributes to achieving transmembrane transport function.
9. The use according to claim 1, wherein said sDSS1 protein or a fragment or variant thereof comprises chemical modifications on 1 to 20 amino acids.
10. The use according to claim 8, wherein said chemical modification comprises amino or glycosylation modification, fatty acid modification, acylation modification, Fc fragment fusion, albumin fusion, pegylation modification, dextran modification, heparin modification, polyvinylpyrrolidone modification, polyamino acid modification, polysialic acid modification, chitosan and its derivative modification, lectin modification, sodium alginate modification, carbomer modification, polyvinylpyrrolidone modification, hydroxypropyl methylcellulose modification, hydroxypropyl cellulose modification, acetylation modification, formylation modification, phosphorylation modification, methylation modification and/or sulfonation modification.

11. The use according to claim 1, wherein said vector comprises a eukaryotic expression plasmid vector, adenovirus, adeno-associated virus, lentivirus, retrovirus, baculovirus, herpes virus, or pseudorabies virus.
12. The use according to claim 1, wherein said cell is any one of a stem cell, a precursor cell or an adult cell of humans.
13. The use according to claim 12, wherein said stem cell is an induced pluripotent stem cell, a cell obtained by transdifferentiation, or a stem cell derived from a primary culture, a pluripotent or unipotent stem cell differentiated from a parent cell.
14. The use according to claim 1, wherein said tissue is a whole organ or a partial tissue mass of a brain, liver, kidney, spleen or pancreatic islets, or blood, fat, muscle, bone marrow or skin.
15. The use according to claim 1, wherein a hypolipidemic drug is to be further administered to the individual.
16. The use according to claim 1, wherein an antihypertensive drug is to be further administered to the individual.
17. The use according to claim 1, wherein an anticoagulant is to be further administered to the individual.
18. The use according to claim 1, wherein said individual undergoes a surgical procedure selected from a group consisting of percutaneous coronary intervention, coronary artery bypass grafting, or carotid endarterectomy.
19. The use according to claim 1, wherein said medicament reduces lipid accumulation in the arterial vessel walls.
20. The use according to claim 10, wherein said lipid comprises one or more of cholesterol, cholesterol ester, triglyceride, chylomicron (CM), low-density lipoprotein (LDL), very low-density lipoprotein (VLDL), intermediate density lipoprotein (IDL), lipoprotein (a) (Lp(a)), oxidized low-density lipoprotein (oxLDL) and the respective metabolic intermediates thereof in the blood.
21. The use according to claim 1, wherein said atherosclerosis or atherosclerosis-related diseases comprise vascular inner diameter stenosis, vascular outer diameter dilation, decreased vasoconstriction and vasodilatation capacity, decreased vascular elasticity, increased vascular fragility, angiolithic degeneration or calcinosis, and thrombus-induced reduction in blood supply capacity of blood vessels.
22. The use according to claim 1, wherein said atherosclerosis or atherosclerosis-related diseases comprise hypertension, angina pectoris, myocardial infarction, myocardium blood-supply insufficiency, arrhythmia, cerebral blood supply insufficiency, cerebral ischemic stroke, cerebral atrophy, renal insufficiency, renal artery stenosis, paralytic ileus, or acral ischemic necrosis.
23. Use of a therapeutically effective amount of sDSS1 protein or a fragment or variant thereof in the manufacture of a medicament for reducing lipid absorption by vascular endothelium in an individual in need thereof.
24. The use according to claim 23, wherein said sDSS1 protein or a fragment or variant thereof has at least 80%, 85%, 90%, 95%, 98%, or 100% sequence identity with the sequence as shown in SEQ ID NO: 1.

25. The use according to claim 23, wherein said sDSS1 protein or a fragment or variant thereof comprises insertion, deletion or substitution of no more than 10, 9, 8, 7, 6, 5, 4, 3, 2 or 1 amino acid(s) compared with the sequence as shown in SEQ ID NO: 1.
26. The use according to claim 23, wherein said sDSS1 protein or a fragment or variant thereof comprises non-natural amino acids.
27. The use according to claim 26, wherein said non-natural amino acids comprise hydroxyproline, hydroxylysine, selenocysteine, D-amino acids, or synthetic non-natural amino acids and derivatives thereof.
28. The use according to claim 23, wherein said sDSS1 protein or a fragment or variant thereof comprises an amino acid sequence as shown in SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO: 10, SEQ ID NO: 11, SEQ ID NO: 12, SEQ ID NO: 13, or SEQ ID NO: 14.
29. The use according to claim 23, wherein said sDSS1 protein or a fragment or variant thereof comprises a fragment having at least 80%, 85%, 90%, 95%, 98%, or 100% sequence identity with the sequence as shown in SEQ ID NO: 17 and a fragment having at least 80%, 85%, 90%, 95%, 98%, or 100% sequence identity with the sequence as shown in SEQ ID NO: 18.
30. Use of a therapeutically effective amount of sDSS1 protein or a fragment or variant thereof in the manufacture of a medicament for reducing lipid accumulation in macrophages in an individual in need thereof.
31. The use according to claim 30, wherein said sDSS1 protein or a fragment or variant thereof has at least 80%, 85%, 90%, 95%, 98%, or 100% sequence identity with the sequence as shown in SEQ ID NO:1.
32. The use according to claim 30, wherein said sDSS1 protein or a fragment or variant thereof comprises insertion, deletion or substitution of no more than 10, 9, 8, 7, 6, 5, 4, 3, 2 or 1 amino acid(s) compared with the sequence as shown in SEQ ID NO: 1.
33. The use according to claim 30, wherein said sDSS1 protein or a fragment or variant thereof comprises non-natural amino acids.
34. The use according to claim 33, wherein said non-natural amino acids comprise hydroxyproline, hydroxylysine, selenocysteine, D-amino acids, or synthetic non-natural amino acids and derivatives thereof.
35. The use according to claim 30, wherein said sDSS1 protein or a fragment or variant thereof comprises an amino acid sequence as shown in SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO: 10, SEQ ID NO: 11, SEQ ID NO: 12, SEQ ID NO: 13, or SEQ ID NO: 14.
36. The use according to claim 30, wherein said sDSS1 protein or a fragment or variant thereof comprises a fragment having at least 80%, 85%, 90%, 95%, 98%, or 100% sequence identity with the sequence as shown in SEQ ID NO: 17 and a fragment having at least 80%, 85%, 90%, 95%, 98%, or 100% sequence identity with the sequence as shown in SEQ ID NO: 18.
37. Use of a therapeutically effective amount of sDSS1 protein or a fragment or variant thereof in the manufacture of a medicament for increasing lipid accumulation in liver cells in an individual in need thereof.

38. The use according to claim 37, wherein said sDSS1 protein or a fragment or variant thereof has at least 80%, 85%, 90%, 95%, 98%, or 100% sequence identity with the sequence as shown in SEQ ID NO: 1.
39. The use according to claim 37, wherein said sDSS1 protein or a fragment or variant thereof comprises insertion, deletion or substitution of no more than 10, 9, 8, 7, 6, 5, 4, 3, 2 or 1 amino acid(s) compared with the sequence as shown in SEQ ID NO: 1.
40. The use according to claim 37, wherein said sDSS1 protein or a fragment or variant thereof comprises non-natural amino acids.
41. The use according to claim 40, wherein said non-natural amino acids comprise hydroxyproline, hydroxylysine, selenocysteine, D-amino acids, or synthetic non-natural amino acids and derivatives thereof.
42. The use according to claim 37, wherein said sDSS1 protein or a fragment or variant thereof comprises an amino acid sequence as shown in SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO: 10, SEQ ID NO: 11, SEQ ID NO: 12, SEQ ID NO: 13, or SEQ ID NO: 14.
43. The use according to claim 37, wherein said sDSS1 protein or a fragment or variant thereof comprises a fragment having at least 80%, 85%, 90%, 95%, 98%, or 100% sequence identity with the sequence as shown in SEQ ID NO: 17 and a fragment having at least 80%, 85%, 90%, 95%, 98%, or 100% sequence identity with the sequence as shown in SEQ ID NO: 18.
44. Use of an effective amount of sDSS1 protein or a fragment or variant thereof, wherein the sDSS1 protein or a fragment or variant thereof can form a complex with free oxidized LDL in the manufacture of a medicament for reducing the amount of circulating oxidized LDL in the blood vessels of an individual.
45. The use according to claim 44, wherein said medicament reduces the amount of free uncomplexed oxidized LDL and the amount of total oxidized LDL.
46. The use according to claim 44, wherein said sDSS1 protein or a fragment or variant thereof has at least 80%, 85%, 90%, 95%, 98%, or 100% sequence identity with the sequence as shown in SEQ ID NO: 1.
47. The use according to claim 44, wherein said sDSS1 protein or a fragment or variant thereof comprises insertion, deletion or substitution of no more than 10, 9, 8, 7, 6, 5, 4, 3, 2 or 1 amino acid(s) compared with the sequence as shown in SEQ ID NO: 1.
48. The use according to claim 44, wherein said sDSS1 protein or a fragment or variant thereof comprises non-natural amino acids.
49. The use according to claim 48, wherein said non-natural amino acids comprise hydroxyproline, hydroxylysine, selenocysteine, D-amino acids, or synthetic non-natural amino acids and derivatives thereof.
50. The use according to claim 44, wherein said sDSS1 protein or a fragment or variant thereof comprises an amino acid sequence as shown in SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO: 10, SEQ ID NO: 11, SEQ ID NO: 12, SEQ ID NO: 13, or SEQ ID NO: 14.
51. The use according to claim 44, wherein said sDSS1 protein or a fragment or variant thereof comprises a fragment having at least 80%, 85%, 90%, 95%, 98%, or 100% sequence identity with the

sequence as shown in SEQ ID NO: 17 and a fragment having at least 80%, 85%, 90%, 95%, 98%, or 100% sequence identity with the sequence as shown in SEQ ID NO: 18.

52. Use of an effective amount of sDSS1 protein or a fragment or variant thereof, wherein the sDSS1 protein or a fragment or variant thereof can form a complex with free oxidized LDL in the manufacture of a medicament for reducing plaque formation in the blood vessels of an individual.

53. The use according to claim 52, wherein said blood vessel is an artery.

54. The use according to claim 52, wherein said blood vessel is an aorta.

55. The use according to claim 52, wherein said sDSS1 protein or a fragment or variant thereof has at least 80%, 85%, 90%, 95%, 98%, or 100% sequence identity with the sequence as shown in SEQ ID NO: 1.

56. The use according to claim 52, wherein said sDSS1 protein or a fragment or variant thereof comprises insertion, deletion or substitution of no more than 10, 9, 8, 7, 6, 5, 4, 3, 2 or 1 amino acid(s) compared with the sequence as shown in SEQ ID NO: 1.

57. The use according to claim 52, wherein said sDSS1 protein or a fragment or variant thereof comprises non-natural amino acids.

58. The use according to claim 57, wherein said non-natural amino acids comprise hydroxyproline, hydroxylysine, selenocysteine, D-amino acids, or synthetic non-natural amino acids and derivatives thereof.

59. The use according to claim 52, wherein said sDSS1 protein or a fragment or variant thereof comprises an amino acid sequence as shown in SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO: 10, SEQ ID NO: 11, SEQ ID NO: 12, SEQ ID NO: 13, or SEQ ID NO: 14.

60. The use according to claim 52, wherein said sDSS1 protein or a fragment or variant thereof comprises a fragment having at least 80%, 85%, 90%, 95%, 98%, or 100% sequence identity with the sequence as shown in SEQ ID NO: 17 and a fragment having at least 80%, 85%, 90%, 95%, 98%, or 100% sequence identity with the sequence as shown in SEQ ID NO: 18.

61. Use of a protein wherein the protein is sDSS1 protein or a fragment or variant thereof in the manufacture of a medicament for sequestering circulating free oxidized LDL in blood vessels in the form of a protein-lipid complex, wherein the oxidized LDL is to be exposed to the protein to form the protein-lipid complex in the blood vessels.

62. The use according to claim 61, wherein said sDSS1 protein or a fragment or variant thereof has at least 80%, 85%, 90%, 95%, 98%, or 100% sequence identity with the sequence as shown in SEQ ID NO: 1.

63. The use according to claim 61, wherein said sDSS1 protein or a fragment or variant thereof comprises insertion, deletion or substitution of no more than 10, 9, 8, 7, 6, 5, 4, 3, 2 or 1 amino acid(s) compared with the sequence as shown in SEQ ID NO: 1.

64. The use according to claim 61, wherein said sDSS1 protein or a fragment or variant thereof comprises non-natural amino acids.

65. The use according to claim 64, wherein said non-natural amino acids comprise hydroxyproline, hydroxylysine, selenocysteine, D-amino acids, or synthetic non-natural amino acids and a derivative thereof.

66. The use according to claim 61, wherein said sDSS1 protein or a fragment or variant thereof comprises an amino acid sequence as shown in SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO: 10, SEQ ID NO: 11, SEQ ID NO: 12, SEQ ID NO: 13, or SEQ ID NO: 14.

67. The use according to claim 61, wherein said sDSS1 protein or a fragment or variant thereof comprises a fragment having at least 80%, 85%, 90%, 95%, 98%, or 100% sequence identity with the sequence as shown in SEQ ID NO: 17 and a fragment having at least 80%, 85%, 90%, 95%, 98%, or 100% sequence identity with the sequence as shown in SEQ ID NO: 18.

68. A complex of sDSS1 protein or a fragment or variant thereof and lipids.

69. A method for screening a therapeutic agent for the treatment of atherosclerosis or atherosclerosis-related diseases in an individual in need thereof, comprising contacting the therapeutic agent with sDSS1 protein, the gene of the sDSS1 protein, the regulatory elements of the sDSS1 gene and the transcription product of the sDSS1 gene, and evaluating the effect of the therapeutic agent on the expression of the sDSS1 protein.