

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 secretory deleted split hand/split foot 1 (sDSS1) as shown in any one of SEQ IDs NO: 1-18 or a vector encoding the sDSS1 protein in the manufacture of a medicament for preventing or treating atherosclerosis in an individual in need thereof.

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

CLAIMS

WHAT IS CLAIMED IS:

1. Use of a therapeutically effective amount of secretory deleted split hand/split foot 1 (sDSS1) protein as shown in any one of SEQ IDs NO: 1-18 or a vector encoding the sDSS1 protein in the manufacture of a medicament for preventing or treating atherosclerosis in an individual in need thereof.
2. The use according to claim 1, wherein said sDSS1 protein comprises non-natural amino acids.
3. 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.
4. The use according to claim 1, wherein said sDSS1 protein comprises chemical modification on 1 to 20 amino acids.
5. The use according to claim 4, 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, 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.
6. 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.
7. The use according to claim 1, wherein a hypolipidemic drug is to be further administered to the individual.
8. The use according to claim 1, wherein an antihypertensive drug is to be further administered to the individual.
9. The use according to claim 1, wherein an anticoagulant is to be further administered to the individual.
10. 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.
11. The use according to claim 1, wherein said medicament reduces lipid accumulation in the arterial vessel walls.
12. The use according to claim 11, 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.

13. The use according to claim 1, wherein said atherosclerosis comprises 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.

14. The use according to claim 1, wherein said atherosclerosis comprises hypertension, angina pectoris, myocardial infarction, arrhythmia, cerebral ischemic stroke, cerebral atrophy, renal insufficiency, renal artery stenosis, paralytic ileus, or acral ischemic necrosis.