

WHAT CLAIMED IS:

1. An MG53 mutant, wherein the MG53 mutant is identical to the amino acid sequence of a wild-type MG53 except for at least one serine in the coiled-coil-SPRY region of the wild-type MG53, which is deleted and/or mutated into ~~any other~~ a non-serine or non-threonine amino acid(s);
wherein the deleted or mutated serine(s) is(are) located at one or more of the following positions of the amino acid sequence of the wild-type MG53: positions 255, 305, 306, and 307; and
~~4.~~ wherein the wild-type MG53 is a human, mouse, rat, monkey, swine, or dog wild-type MG53, the MG53 mutant has an amino acid sequence having at least 90% homology to any one of the amino acid sequences set forth in SEQ ID NOs: 7-12 or 147-150, and the MG53 mutant avoids or reduces metabolic side effects compared to the wild-type MG53, while still retaining cell repair function and/or cardioprotective function.
2. The MG53 mutant according to claim 1, wherein the coiled-coil-SPRY region is located at positions 122-477 of the amino acid sequence of the wild-type MG53.
3. The MG53 mutant according to claim 1 or 2, wherein the amino acid sequence of the wild-type MG53 is set forth in SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5 ~~or~~, SEQ ID NO: 6, SEQ ID NO: 139, SEQ ID NO: 140, SEQ ID NO: 141, or SEQ ID NO: 142.
4. The MG53 mutant according to any one of claims 1 to 3, wherein the serine is mutated into a non-polar amino acid.
5. The MG53 mutant according to claim 4, wherein the non-polar amino acid is selected from the group consisting of glycine, alanine, leucine, isoleucine, valine, proline, phenylalanine, methionine and tryptophan.
6. The MG53 mutant according to claim 5, wherein the non-polar amino acid is alanine.
7. The MG53 mutant according to any one of claims 1 to 6, wherein the serine is mutated into a non-serine or non-threonine polar amino acid.
8. The MG53 mutant according to claim 7, wherein the polar amino acid is selected from the group consisting of glutamine, cysteine, asparagine, tyrosine, aspartic acid, glutamic acid, lysine, arginine and histidine.
9. The MG53 mutant according to claim 8, wherein the polar amino acid is cysteine.

- ~~10. The MG53 mutant according to any one of claims 1 to 9, wherein the deleted or mutated serine is located at one or more of the following positions of the amino acid sequence of the wild type MG53: positions 189, 211, 214, 246, 255, 269, 296, 301, 305, 307, 341, 377, 418, 430.~~
- ~~11. The MG53 mutant according to any one of claims 1 to 10, wherein the deleted or mutated serine is located at one or more of the following positions of the amino acid sequence of the wild type MG53: positions 211, 214, 246, 255, 269, 296, 297.~~
- ~~12.10.~~ The MG53 mutant according to any one of claims 1 to ~~11~~9, wherein the deleted or mutated serine is located at position 255 of the amino acid sequence of the wild-type MG53, or the deleted or mutated serines are located at positions 305, 306 and 307 of the amino acid sequence of the wild-type MG53.
- ~~13.11.~~ The MG53 mutant according to claim ~~12.10~~9, wherein the MG53 mutant has two or more serine mutations.
- ~~14.12.~~ The MG53 mutant according to any one of claims 1 to ~~13.11~~9, wherein the MG53 mutant has an amino acid sequence having at least ~~70~~95% homology to any one of the amino acid sequences set forth in SEQ ID NOs: 7-12 or 147-150, ~~and the MG53 mutant avoids metabolic side effects caused by wild type MG53, while still retaining cell repair function and/or cardioprotective function.~~
- ~~15.13.~~ ~~The MG53 mutant according to any one of claims 1 to 14~~A MG53 mutant, wherein the amino acid sequence of the MG53 mutant is any one of the amino acid sequences set forth in SEQ ID NOs: 7-12 or 147-150.
- ~~16.14.~~ The MG53 mutant according to ~~any one of claims 13 to 15~~, wherein the amino acid sequence of the MG53 mutant is the amino acid sequence set forth in SEQ ID NO: 7.
- ~~17.15.~~ A pharmaceutical composition comprising the MG53 mutant of any one of claims 1 to ~~16.14~~9 and a pharmaceutically acceptable carrier.
- ~~18.16.~~ An isolated nucleic acid comprising a nucleic acid sequence encoding the amino acid sequence of the MG53 mutant of any one of claims 1 to ~~16.14~~9.
- ~~19.17.~~ The nucleic acid according to claim ~~18.16~~9 comprising any one of the nucleic acid sequences set forth in SEQ ID NOs: 13-18 or 151-154.
- ~~20.18.~~ An expression vector comprising the nucleic acid sequence according to claim ~~18.16~~9.
- ~~21.19.~~ The expression vector according to claim ~~20.18~~9 comprising any one of the nucleic acid sequences set forth in SEQ ID NOs: 13-18 or 151-154.

~~22-20.~~ 20-18 or 21-19. A host cell comprising the expression vector according to claim ~~20-18~~ or ~~21-19~~.

~~23-21.~~ 16-14. A method for preparing the MG53 mutant according to any one of claims 1 to ~~16-14~~, comprising determining one or more serine positions for mutation, performing site-directed mutagenesis at the position on the full-length sequence of a plasmid comprising the nucleic acid sequence encoding the amino acid sequence of wild-type MG53, transfecting the plasmid with site-directed mutagenesis into a host cell, and inducing the host cell to produce the MG53 mutant.

~~24-22.~~ 23-21. The method according to claim ~~23-21~~, wherein the site-directed mutagenesis comprises the following steps:

- (1) determining the corresponding nucleotide site of the amino acid targeted for site-directed mutagenesis in the cDNA sequence, modifying the nucleotide sequence at the mutation site according to the target amino acid, and designing primers by intercepting a sequence of 20-40 bp in length comprising the mutation site;
- (2) performing PCR reaction by using the primers of step (1) and taking a wild-type MG53 plasmid as a template, performing agarose gel electrophoresis for the PCR product, and purifying the PCR product;
- (3) performing enzymatic reaction for the purified PCR product of step (2) by using restriction endonuclease, ligating the enzyme-digested product with a suitable plasmid expression vector, transforming and cultivating the ligation product in bacterial competent cells;
- (4) selecting the clones of step (3) to perform colony PCR identification by using the primers of step (1), performing agarose gel electrophoresis for the PCR product, and then performing DNA sequencing identification to identify positive clones with the site-directed mutagenesis.

~~25-23.~~ 16-14. Use of the MG53 mutant according to any one of claims 1 to ~~16-14~~ in the manufacture of a medicament for treating heart diseases, diabetic cerebrovascular diseases, diabetic ocular complications, diabetic neuropathy, diabetic foot, kidney diseases, and diseases associated with cellular and/or tissue damage.

~~26-24.~~ 25-23. The use according to claim ~~25-23~~, wherein the medicament avoids metabolic side effects while treating heart diseases, diabetic cerebrovascular diseases, diabetic ocular complications, diabetic neuropathy, diabetic foot, kidney diseases, and diseases associated with cellular and/or tissue damage.

- ~~27~~25. The use according to claim ~~25-23~~ or ~~26~~24, wherein the heart diseases are diseases associated with myocardial damage.
- ~~28~~26. The use according to any one of claims ~~25-23~~ to ~~27~~25, wherein the heart diseases comprise diabetic heart disease, myocardial ischemia, cardiac ischemia/reperfusion injury, myocardial infarction, heart failure, arrhythmia, heart rupture, angina, myocarditis, coronary heart disease and pericarditis.
- ~~29~~27. The use according to claim ~~25-23~~ or ~~26~~24, wherein the diabetic cerebrovascular diseases comprise cerebral arteriosclerosis, ischemic cerebrovascular disease, cerebral hemorrhage, cerebral atrophy and cerebral infarction.
- ~~30~~28. The use according to claim ~~25-23~~ or ~~26~~24, wherein the diabetic ocular complications comprise diabetic retinopathy, diabetic cataract, diabetic associated uveitis and blindness.
- ~~31~~29. The use according to claim ~~25-23~~ or ~~26~~24, wherein the diabetic neuropathy comprises diabetic peripheral neuropathy.
- ~~32~~30. The use according to claim ~~25-23~~ or ~~26~~24, wherein the kidney diseases include acute glomerulonephritis, chronic glomerulonephritis, nephrotic syndrome, acute kidney injury and diabetic nephropathy.
- ~~33~~31. The use according to claim ~~25-23~~ or ~~26~~24, wherein the diseases associated with cellular and/or tissue damage comprise diseases associated with the damage of kidney, brain, lung, liver, heart, spleen, digestive tract and skin.
- ~~34~~32. The use according to claim ~~33~~31, wherein the diseases associated with cellular and/or tissue damage comprise trauma, burns, ulcers, mucositis, asthma, chronic obstructive pulmonary disease, stroke and skin aging.
- ~~35~~33. The use according to any one of claims ~~25-23~~ to ~~34~~32, wherein the amino acid sequence of the MG53 mutant is the amino acid sequence set forth in SEQ ID NO: 7.