CLAIMS

1. Modified mitochondria in which a foreign protein is bound to the outer membrane of the mitochondria.

2. The modified mitochondria according to claim 1, wherein the mitochondria are isolated from cells or tissues.

3. The modified mitochondria according to claim 2, wherein the cell is any one selected from the group consisting of somatic cells, germ cells, stem cells, and a combination thereof.

4. The modified mitochondria according to claim 1, wherein the foreign protein comprises a desired protein capable of functioning inside and outside the cell.

5. The modified mitochondria according to claim 1, wherein the foreign protein comprises a mitochondria anchoring peptide.

6. The modified mitochondria according to claim 5, wherein the foreign protein is bound to the outer membrane of the mitochondria by a mitochondria anchoring peptide.

7. The modified mitochondria according to claim 6, wherein the mitochondria anchoring peptide comprises an N terminal region or a C terminal region of a protein present in the mitochondrial membrane protein.

8. The modified mitochondria according to claim 7, characterized in that the N terminal region or the C terminal region of the protein present in the mitochondrial membrane protein is located on the outer membrane of the mitochondria.

9. The modified mitochondria according to claim 7, characterized in that the protein present in the mitochondrial membrane protein is any one selected from the group consisting of TOM20, TOM70, OM45, TOM5, TOM6, TOM7, TOM22, Fis1, Bcl-2, Bcl-x and VAMP1B.

10. The modified mitochondria according to claim 7, characterized in that the anchoring peptide comprises an N terminal region of any one selected from the group consisting of TOM20, TOM70 and OM45.

11. The modified mitochondria according to claim 7, characterized in that the mitochondria anchoring peptide comprises a C terminal region of any one selected from the group consisting of TOM5, TOM6, TOM7, TOM22, Fis1, Bcl-2, Bcl-x and VAMP1B.

12. The modified mitochondria according to claim 1, wherein the foreign protein is a fusion protein comprising a mitochondria anchoring peptide and a desired protein capable of functioning inside and outside the cell.

13. The modified mitochondria according to claim 12, wherein the desired protein is any one selected from the group consisting of an active protein exhibiting an activity in a cell, a protein present in a cell, and a protein having the ability to bind to a ligand or receptor present in a cell membrane.

14. The modified mitochondria according to claim 13, wherein the desired protein is any one selected from the group consisting of p53, Granzyme B, Bax, Bak, PDCD5, E2F, AP-1(Jun/Fos), EGR-1, Retinoblastoma(RB), phosphatase and tensin homolog(PTEN), E-cadherin, Neurofibromin-2(NF-2), poly[ADP-ribose] synthase 1(PARP-1), BRCA-1, BRCA-2, Adenomatous polyposis coli(APC), Tumor necrosis factor receptor-associated factor(TRAF), RAF kinase inhibitory protein(RKIP), p16, KLF-10, LKB1, LHX6, C-RASSF, DKK-3PD1, Oct3/4, Sox2, Klf4, and c-Myc.

15. The modified mitochondria according to claim 12, wherein the foreign protein is a desired protein bound to the N terminal region of TOM20, TOM70 or OM45.

16. The modified mitochondria according to claim 15, wherein the foreign protein is bound in the following order:
N terminal-N terminal region of TOM20, TOM70 or OM45-desired protein-C terminal.

17. The modified mitochondria according to claim 16, wherein the foreign protein further comprises an amino acid sequence recognized by a proteolytic enzyme in eukaryotic cells, or ubiquitin or a fragment thereof between the anchoring peptide and the desired protein.

18. The modified mitochondria according to claim 17, wherein the ubiquitin fragment comprises the C terminal Gly-Gly of an amino acid sequence of SEQ ID NO: 71, and comprises 3 to 75 amino acids consecutive from the C terminal.

19. The modified mitochondria according to claim 17, wherein the foreign protein further comprises a linker between a desired protein and ubiquitin or a fragment thereof.

20. The modified mitochondria according to claim 19, wherein the linker is composed of 1 to 150 amino acids.

21. The modified mitochondria according to claim 20, wherein the linker is composed of 5 to 50 amino acids consisting of glycine and serine.

22. The modified mitochondria according to claim 21, wherein the linker is (G4S)n, in which n is an integer of 1 to 10.

23. The modified mitochondria according to claim 13, wherein the protein having the ability to bind to a ligand or receptor present in a cell membrane is a ligand or receptor present on the surface of a tumor cell.

24. The modified mitochondria according to claim 23, wherein the ligand or receptor present on the surface of a tumor cell is any one selected from the group consisting of CD19, CD20, melanoma antigen E(MAGE), NY-ESO-1, carcinoembryonic antigen(CEA), mucin 1 cell surface associated(MUC-1), prostatic acid phosphatase(PAP), prostate specific antigen(PSA), survivin, tyrosine related protein 1(tyrp1), tyrosine related protein 1(tyrp2), Brachyury, Mesothelin, Epidermal growth factor receptor(EGFR), human epidermal growth factor receptor 2(HER-2), ERBB2, Wilms tumor protein(WT1), FAP, EpCAM, PD-L1, ACPP, CPT1A, IFNG, CD274, FOLR1, EPCAM, ICAM2, NCAM1, LRRC4, UNC5H2 LILRB2, CEACAM, Nectin-3, or a combination thereof.

25. The modified mitochondria according to claim 12, wherein the foreign protein is bound to a C terminal region of any one selected from the group consisting of TOM5, TOM6, TOM7, TOM22, Fis1, Bcl-2, Bcl-x and VAMP1B.

26. The modified mitochondria according to claim 25, wherein the foreign protein is bound in the following order:
N terminal-desired protein-C terminal region of any one selected from the group consisting of TOM5, TOM6, TOM7, TOM22, Fis1, Bcl-2, Bcl-x and VAMP1B-C terminal.

27. The modified mitochondria according to claim 26, wherein the foreign protein further comprises a linker between the desired protein and the C terminal region of any one selected from the group consisting of TOM5, TOM6, TOM7, TOM22, Fis1, Bcl-2, Bcl-x and VAMP1B.

28. The modified mitochondria according to claim 27, wherein the linker is composed of 1 to 150 amino acids.

29. The modified mitochondria according to claim 28, wherein the linker is composed of 5 to 50 amino acids consisting of glycine and serine.

30. The modified mitochondria according to claim 21, wherein the linker is (G4S)n, in which n is an integer of 1 to 10.

31. A pharmaceutical composition comprising a modified mitochondria according to any of claims 1 to 30 as an active ingredient.

32. The pharmaceutical composition according to claim 31, wherein the pharmaceutical composition is for the prevention or treatment of cancer.

33. The pharmaceutical composition according to claim 32, wherein the cancer is any one selected from the group consisting of gastric cancer, liver cancer, lung cancer, colorectal cancer, breast cancer, prostate cancer, ovarian cancer, pancreatic cancer, cervical cancer, thyroid cancer, larynx cancer, acute myeloid leukemia, brain tumor, neuroblastoma,

retinoblastoma, head and neck cancer, salivary gland cancer and lymphoma.

34. Use of a modified mitochondria as a means of intracellular and extracellular delivery of a foreign protein comprising a desired protein capable of functioning inside and outside the cell.

35. The use of the modified mitochondria according to claim 34, wherein the foreign protein comprises a mitochondrial outer membrane anchoring peptide, and is bound to the outer membrane of the mitochondria by the outer membrane anchoring peptide, and is delivered inside and outside the cell.

36. A fusion protein comprising a mitochondrial outer membrane anchoring peptide and a desired protein capable of functioning inside and outside the cell.

37. The fusion protein according to claim 36, wherein the mitochondrial outer membrane anchoring peptide comprises an N terminal or C terminal sequence of a protein present in the outer membrane of mitochondria.

38. The fusion protein according to claim 36, wherein the mitochondrial outer membrane anchoring peptide is any one selected from the group consisting of TOM20, TOM70, OM45, TOM5, TOM6, TOM7, TOM22, Fis1, Bcl-2, Bcl-x and VAMP1B.

39. The fusion protein according to claim 36, wherein the desired protein is any one selected from the group consisting of p53, Granzyme B, Bax, Bak, PDCD5, E2F, AP-1(Jun/Fos), EGR-1, Retinoblastoma(RB), phosphatase and tensin homolog(PTEN), E-cadherin, Neurofibromin-2(NF-2), poly[ADP-ribose] synthase 1(PARP-1), BRCA-1, BRCA-2, Adenomatous polyposis coli(APC), Tumor necrosis factor receptor-associated factor(TRAF), RAF kinase inhibitory protein(RKIP), p16, KLF-10, LKB1, LHX6, C-RASSF, DKK-3PD1, Oct3/4, Sox2, Klf4, and c-Myc.

40. The fusion protein according to claim 36, wherein when the mitochondrial outer membrane anchoring peptide is TOM20, TOM70 or OM45, the mitochondrial outer membrane anchoring peptide and the desired protein are bound from the N terminal to the C terminal.

41. The fusion protein according to claim 36, wherein when the mitochondrial outer membrane anchoring peptide is any one selected from the group consisting of TOM5, TOM6, TOM7, TOM22, Fis1, Bcl-2, Bcl-x and VAMP1B, the desired protein and the mitochondrial outer membrane anchoring peptide are bound from the N terminal to the C terminal.

42. The fusion protein according to claim 36, wherein the fusion protein further comprises ubiquitin or a fragment thereof between the mitochondrial outer membrane anchoring peptide and the desired protein.

43. The fusion protein according to claim 36, wherein the fusion protein further comprises an amino acid sequence recognized by a proteolytic enzyme in eukaryotic cells between the mitochondrial outer membrane anchoring peptide and the desired protein.

44. A polynucleotide encoding the fusion protein according to any one of claims 36 to 43.

45. A method for preparing the fusion protein according to any one of claims 36 to 43, comprising

a step of transforming the polynucleotide according to claim 44 into prokaryotic cells, or eukaryotic cells without a ubiquitin degrading enzyme or a proteolytic enzyme in eukaryotic cells; and

a step of obtaining a fusion protein.

46. A fusion protein comprising the target targeting protein having the ability to bind to a ligand or receptor present in a cell membrane and the mitochondrial outer membrane anchoring peptide.

47. The fusion protein according to claim 46, wherein the mitochondrial outer membrane anchoring peptide is any one selected from the group consisting of TOM5, TOM6, TOM7, TOM22, Fis1, Bcl-2, Bcl-x and VAMP1B.

48. The fusion protein according to claim 46, wherein the target targeting protein having the ability to bind to a ligand or receptor present in a cell membrane and the mitochondrial outer membrane anchoring peptide are bound from the N terminal to the C terminal.

49. The fusion protein according to claim 48, wherein the target targeting protein having the ability to bind to a ligand or receptor present in a cell membrane is an antibody or a fragment thereof.

50. The fusion protein according to claim 49, wherein the fragment of the antibody is any one selected from the group consisting of Fab, Fab', scFv and F (ab)2.

51. A polynucleotide encoding the fusion protein according to any one of claims 46 to 50.

52. A method for preparing modified mitochondria, comprising a step of mixing the isolated mitochondria with the fusion protein according to any one of claims 36 to 43 and/or the fusion protein according to any one of claims 46 to 50.

53. A method for preparing modified mitochondria from the transformed cells by injecting a polynucleotide encoding the fusion protein according to any one of claims 36 to 41 and/or the fusion protein according to any one of claims 46 to 50 into eukaryotic cells.

CLAIMS

1. Modified mitochondria in which a foreign protein is bound to the outer membrane of the mitochondria,

wherein the mitochondria are isolated from cells or tissues,

wherein the foreign protein comprises a mitochondria anchoring peptide and a desired protein capable of functioning inside and outside the cell,

wherein the foreign protein is bound to the outer membrane of the mitochondria by a mitochondria anchoring peptide,

wherein the foreign protein comprises an amino acid sequence recognized by a proteolytic enzyme in eukaryotic cells, or ubiquitin or a fragment thereof between the anchoring peptide and the desired protein,

wherein the mitochondria anchoring peptide is a peptide comprising an anchoring sequence of an N terminal region or a C terminal region of a protein which is located on the outer membrane of the mitochondria and is any one selected from the group consisting of TOM20, TOM70, OM45, TOM5, TOM6, TOM7, TOM22, Fis1, Bcl-2, Bcl-x and VAMP1B.

2. The modified mitochondria according to claim 1, wherein the mitochondria is derived from any one selected from the group consisting of somatic cells, germ cells, stem cells, and a combination thereof.

3. The modified mitochondria according to claim 1, wherein the mitochondria anchoring peptide is the peptide comprising the anchoring sequence of the N terminal region of a protein which is located on the outer membrane of the mitochondria and is any one selected from the group consisting of TOM20, TOM70 and OM45.

4. The modified mitochondria according to claim 1, wherein the mitochondria anchoring peptide is the peptide comprising the anchoring sequence of the C terminal region of a protein which is located on the outer membrane of the mitochondria and is any one selected from the group consisting of TOM5, TOM6, TOM7, TOM22, Fis1, Bcl-2, Bcl-x and VAMP1B.

5. The modified mitochondria according to claim 1, wherein the desired protein is any one selected from the group consisting of an active protein exhibiting an activity in a cell, a protein present in a cell, and a protein having the ability to bind to a ligand or receptor present in a cell

membrane.

6. The modified mitochondria according to claim 5, wherein the desired protein is any one selected from the group consisting of p53, Granzyme B, Bax, Bak, PDCD5, E2F, AP-1(Jun/Fos), EGR-1, Retinoblastoma(RB), phosphatase and tensin homolog(PTEN), E-cadherin, Neurofibromin-2(NF-2), poly[ADP-ribose] synthase 1(PARP-1), BRCA-1, BRCA-2, Adenomatous polyposis coli(APC), Tumor necrosis factor receptor-associated factor(TRAF), RAF kinase inhibitory protein(RKIP), p16, KLF-10, LKB1, LHX6, C-RASSF, DKK-3PD1, Oct3/4, Sox2, Klf4, and c-Myc.

7. The modified mitochondria according to claim 1, wherein the foreign protein is a desired protein bound to the peptide comprising the anchoring sequence of the N terminal region of a protein which is located on the outer membrane of the mitochondria and is TOM20, TOM70 or OM45.

8. The modified mitochondria according to claim 7, wherein the foreign protein is bound in the following order:
N terminal - the peptide comprising the anchoring sequence of the N terminal region of a protein which is located on the outer membrane of the mitochondria and is TOM20, TOM70 or OM45 - desired protein - C terminal.

9. The modified mitochondria according to claim 1, wherein the ubiquitin fragment comprises the C terminal Gly-Gly of an amino acid sequence of SEQ ID NO: 71, and comprises 3 to 75 amino acids consecutive from the C terminal.

10. The modified mitochondria according to claim 1, wherein the foreign protein further comprises a linker between a desired protein and ubiquitin or a fragment thereof.

11. The modified mitochondria according to claim 10, wherein the linker is composed of 1 to 150 amino acids.

12. The modified mitochondria according to claim 11, wherein the linker is composed of 5 to 50 amino acids consisting of glycine and serine.

13. The modified mitochondria according to claim 12, wherein the linker is (G4S)n, in which n is an integer of 1 to 10.

14. The modified mitochondria according to claim 5, wherein the protein having the ability to bind to a ligand or receptor present in a cell membrane is a ligand or receptor present on the surface of a tumor cell.

15. The modified mitochondria according to claim 14, wherein the ligand or receptor present on the surface of a tumor cell is any one selected from the group consisting of CD19, CD20, melanoma antigen E(MAGE), NY-ESO-1, carcinoembryonic antigen(CEA), mucin 1 cell surface associated(MUC-1), prostatic acid phosphatase(PAP), prostate specific antigen(PSA), survivin, tyrosine related protein 1(tyrp1), tyrosine related protein 1(tyrp2), Brachyury, Mesothelin, Epidermal growth factor receptor(EGFR), human epidermal growth factor receptor 2(HER-2), ERBB2, Wilms tumor protein(WT1), FAP, EpCAM, PD-L1, ACPP, CPT1A, IFNG, CD274, FOLR1, EPCAM, ICAM2, NCAM1, LRRC4, UNC5H2 LILRB2, CEACAM, Nectin-3, or a combination thereof.

16. The modified mitochondria according to claim 1, wherein the foreign protein is bound to the peptide comprising the anchoring sequence of the C terminal region of a protein which is located on the outer membrane of the mitochondria and is any one selected from the group consisting of TOM5, TOM6, TOM7, TOM22, Fis1, Bcl-2, Bcl-x and VAMP1B.

17. The modified mitochondria according to claim 16, wherein the foreign protein is bound in the following order:
N terminal-desired protein - the peptide comprising the anchoring sequence of the C terminal region of a protein which is located on the outer membrane of the mitochondria and is any one selected from the group consisting of TOM5, TOM6, TOM7, TOM22, Fis1, Bcl-2, Bcl-x and VAMP1B - C terminal.

18. The modified mitochondria according to claim 17, wherein the foreign protein further comprises a linker between the desired protein and the anchoring sequence of the C terminal region of a protein which is located on the outer membrane of the mitochondria and is any one selected from the group consisting of TOM5, TOM6, TOM7, TOM22, Fis1, Bcl-2, Bcl-x and VAMP1B.

19. The modified mitochondria according to claim 18, wherein the linker is composed of 1 to 150 amino acids.

20. The modified mitochondria according to claim 19, wherein the linker is composed of 5 to 50 amino acids consisting of glycine and serine.

21. The modified mitochondria according to claim 20, wherein the linker is (G4S)n, in which n is an integer of 1 to 10.

22. A pharmaceutical composition for the prevention or treatment of cancer, comprising a modified mitochondria according to any of claims 1, 3, 10, 11, 13 to 16, and 18 to 30 as an active ingredient.

23. The pharmaceutical composition according to claim 22, wherein the cancer is any one selected from the group consisting of gastric cancer, liver cancer, lung cancer, colorectal cancer, breast cancer, prostate cancer, ovarian cancer, pancreatic cancer, cervical cancer, thyroid cancer, larynx cancer, acute myeloid leukemia, brain tumor, neuroblastoma, retinoblastoma, head and neck cancer, salivary gland cancer and lymphoma.