less immunogenic than any foreign delivery vehicle. More importantly, exosomes are natural carriers for miRNAs and other non-coding RNAs, and the direct membrane fusion with the target cell allows contents to be delivered directly into the cytosol. This makes exosomes an excellent delivery system for small molecules.

[010] miRNAs induce gene silencing by partial sequence homology, thus a single miRNA can have hundreds of targets. The role of a miRNA, as an oncogene and/or tumor suppressor, is dependent on its mRNA targets. miRNAs are secreted through exosomes and play an important role in intracellular communication by mediating mRNA repression in neighboring or distant cells. Further, aberrantly expressed miRNAs have been described in various types of tumors. The expression and function of miRNAs have been studied with regards to tumorigenesis, patient prognosis, and as novel therapeutic targets. The most appealing advantage of using miRNAs for the treatment of cancer is their ability to affect multiple target genes in the context of a network, making them especially suitable to treat glioma as it is a complex heterogeneous tumor. Moreover, several in-vitro and pre-clinical studies demonstrated the therapeutic benefits of targeting miRNAs.

[011] In addition to miRNAs, the human genome expresses tens of thousands of long non-coding RNAs (lncRNAs). These non-coding RNAs are >200 bases in length but lack significant open reading frame. lncRNAs exhibit diverse transcriptional patterns, exhibit tissue specificity and play important functions in various cellular processes in both physiological and pathological conditions.

[012] There remains a need for a method of identifying, isolating and/or tailoring specific MSC populations and therapeutic effects. The miRNA, lncRNA and protein characteristics of these cells and their secretome provide information that allows for a more educated targeted and specific MSC therapy for a wide range of diseases.

SUMMARY

[013] The present disclosure provides compositions comprising different sources and subpopulations of mesenchymal stem cells (MSCs) and/or extracellular vesicles secreted from said MSCs, kits comprising same and therapeutic use thereof.

[014] The present disclosure further relates to treating various diseases or conditions with MSCs having unique expression profiles disclosed herein as well as with extracellular vesicles secreted from said MSCs.

[015] Disclosed is a method of treating a disease or condition in a subject in need thereof, the method comprising:

(a) providing an enriched population of chorionic placenta-derived mesenchymal stem cells (CH-MSCs); and

(b) administering to the subject a pharmaceutical composition comprising a therapeutically effecting amount of at least one of:

i. the CH-MSC population;

ii. extracellular vesicles derived from the CH-MSC population;

iii. conditioned media from the CH-MSC population; and

iv. extracellular matrix secreted by the CH-MSC population;

thereby treating the disease or condition.

[015a] According to one aspect, there is provided use of a pharmaceutical composition comprising a therapeutically effecting amount of at least one of:

i. an enriched population of chorionic placenta-derived mesenchymal stem cells (CH-MSCs);

ii. extracellular vesicles derived from said CH-MSC population;

iii. conditioned media from said CH-MSC population; and

iv. extracellular matrix secreted by said CH-MSC population;

in the manufacture of a medicament for treating a disease or condition in a subject in need thereof.

[016] According to another aspect, there is provided a method of selecting a mesenchymal stem cell (MSC) subpopulation, the method comprising:

(a) providing MSCs; and

(b) selecting at least one MSC expressing of at least one surface marker on the at least one MSC's surface, wherein expression of at least one of CD184, CD193, CD235a, CD318, CD255, CD268, fMLP, ITGA2, ITGA4, and CD326 indicates an MSC is an umbilical cord-derived MSC, expression of at least one of TCR alpha-beta, CD55, LIFR, ST6GALNACS, and MIC A/B indicates an MSC is a chorionic placenta-derived MSC, expression of at least one of CD24, CD48, CD66b, CD338, CD120b, CD268, FGFLR1, ITGA5, NES, and PDGFRAA indicates an MSC is a bone marrow-derived MSC, expression of at least one of CD84, PDGFRBB, and TNFRSF11B indicates an MSC is an adipose-derived MSC, and expression of CD157 indicates an MSC is an amniotic placenta-derived MSC;

thereby selecting an MSC subpopulation.

[017] According to another aspect, there is provided a pharmaceutical composition for use in treating a disease or condition comprising a pharmaceutically acceptable adjuvant, excipient or carrier and at least one of:

[023] According to some embodiments, the autoimmune disease is selected from MS, diabetes, colitis, and Chron's disease.

[024] According to some embodiments, the energy homeostasis disease is diabetes.

[025] According to some embodiments, the digestive disease is selected from irritable bowel syndrome (IBD), Chron's disease, and colitis.

[026] According to some embodiments, aging comprises at least one of skin aging, muscle aging, and brain aging.

[027] According to some embodiments, the proliferative disease is cancer. According to some embodiments, the cancer is any one of brain cancer, metastasis to the brain, lung cancer, breast cancer, colon cancer, pancreatic cancer, prostate cancer, and head and neck cancer. According to some embodiments, the brain cancer is selected from glioma, medulloblastoma, neuroblastoma and meningioma. According to some embodiments, the glioma is glioblastoma. According to some embodiments, the MSC population, extracellular vesicles, conditioned media, extracellular matrix or a combination thereof comprise at least one of miR-145 and miR-656. According to some embodiments, the methods of the disclosure further comprise irradiating the subject.

[028] According to some embodiments, the enriched population of CH-MSCs is substantially devoid of amniotic placenta-derived MSCs (AM-MSCs).

[029] According to some embodiments, the providing comprises, selecting CH-MSCs from a mix of cells or placental tissue. According to some embodiments, the selecting comprises selecting at least one cell expressing at least one surface marker selected from TCR alpha-beta, CD55, LIFR, ST6GALNACS, and MIC A/B.

[030] According to some embodiments, the administering comprises at least one of intravenous administration, intramuscular administration, intranasal administration, intrathecal administration, intrastriatal administration, intracranial administration, intraarterial administration, and subcutaneous administration.

[031] According to some embodiments, the CH-MSC population is allogenic to the subject. According to some embodiments, the CH-MSC population is autologous to the subject.

[032] According to some embodiments, the methods of the disclosure further comprise confirming expression of the at least one surface marker on the surface of the selected CH-MSC.

[033] According to some embodiments, the methods of the disclosure further comprise culturing the MSC in MSC growth media.

[034] According to some embodiments, the providing comprises providing tissue or a cell mixture and isolating MSCs from the tissue or cell mixture.

[035] According to some embodiments, the isolating MSCs comprises isolation of cells expressing a plurality of surface marker selected from CD9, CD10, CD13, CD26, CD29, CD44, CD36, CD46, CD47, CD49a, CD49b, CD49c, CD49d, CD49e, CD50, CD51/61, CD54, CD55, CD58, CD59, CD61, CD63, CD71, CD73, CD81, CD83, CD87, CD90, CD91, CD95, CD97, CD98, CD99, CD105, CD108, CD109, CD140b, CD142, CD146, CD147, CD151, CD164, CD165, CD166, CD273, β2-microglobulin, HLA-A,B,C, HLA-A2, and STRO1.

[036] According to some embodiments, the tissue is selected from placenta, umbilical cord, adipose tissue and bone marrow.

[037] According to some embodiments, the methods of the disclosure further comprise confirming expression of the at least one surface marker on the surface of the selected MSC.

[038] According to some embodiments, the culture medium comprises conditioned media from the MSC. According to some embodiments, the culture medium comprises extracellular matrix from the MSC.

[039] According to some embodiments, the growing comprises coculture of the stem cells, primary cells or both with the MSC.

[040] According to some embodiments, the methods of the disclosure further comprise growing the stem cells, primary cells or both in primary cell growth media.

[041] According to some embodiments, the maintaining comprises extending survival of the stem cells, primary cells or both beyond survival of the cells in culture medium substantially devoid of extracellular vesicles from the MSC. According to some embodiments, the maintaining comprises culturing the stem cells, primary cells or both in vitro for at least 10 passages. According to some embodiments, the maintaining comprises the stem cells, primary cells or both retaining the ability to undergo both symmetric and asymmetric divisions.

[042] According to some embodiments, the MSCs are umbilical cord-derived MSCs (UC-MSCs), CH-MSCs or a combination thereof. According to some embodiments, the MSCs are CH-MSCs.

[043] According to some embodiments, the stem cell are cancer stem cells and the MSCs are bone marrow-derived MSCs, (BM-MSCs), adipose-derived MSCs (AD-MSCs), AM-MSCs, or a combination thereof.

[044] According to another aspect, there is provided a pharmaceutical composition comprising at least one of: a mesenchymal stem cell (MSC) population, extracellular vesicles secreted from the MSC population, conditioned media from the MSC population and a combination thereof; the MSC population is characterized by an expression profile selected from any one of Tables 1-5.

[045] According to some embodiments, the pharmaceutical compositions of the disclosure further comprise a pharmaceutically acceptable carrier.

[046] Further embodiments and the full scope of applicability of the present disclosure will become apparent from the detailed description given hereinafter. However, it should be understood that the detailed description and specific examples, while indicating preferred embodiments of the disclosure, are given by way of illustration only, since various changes and modifications within the spirit and scope of the disclosure will become apparent to those skilled in the art from this detailed description.

BRIEF DESCRIPTION OF THE DRAWINGS

[047] **Figures 1A-C. Different MSC populations and their exosomes have opposite effects on glioma stem cells. (1A)** A bar chart of self-renewal of glioblastoma cells after incubation with MSC subtypes. Self-renewal is represented as a percentage of the self-renewal when cells were incubated with control. **(1B)** A bar chart of self-renewal of glioblastoma cells after incubation with exosomes from various MSC subtypes. Self-renewal is represented as a percentage of the self-renewal when cells were incubated with control. **(1C)** A bar chart of relative mRNA expression levels of five mesenchymal and stemness markers in five MSC subtypes. Control expression was standardized to 1. The populations for each gene are presented in the following order: Control, UC, CH, AM, BM, AD.

[048] **Figures 2A-H. MSC Population and their exosomes inhibit glioblastoma and prolong survival.** (**2A**) A bar chart, showing survival, as measured in days, of mice receiving four different MSC subtypes or control cells. **(2B)** A bar chart, showing survival, as measured in days, of mice

CLAIMS

1. Use of a pharmaceutical composition comprising a therapeutically effecting amount of at least one of:

    i. an enriched population of chorionic placenta-derived mesenchymal stem cells (CH-MSCs);

    ii. extracellular vesicles derived from said CH-MSC population;

    iii. conditioned media from said CH-MSC population; and

    iv. extracellular matrix secreted by said CH-MSC population;

    in the manufacture of a medicament for treating a disease or condition in a subject in need thereof.

2. The use of claim 1, wherein said disease or condition is selected from a neurological disease, a muscular disease, an autoimmune disease, an inflammatory disease, a digestive disease, an energy homeostasis disease, a fibrotic disease, aging, radiation induced injury, cell transplant rejection and a proliferative disease.

3. The use of claim 2, wherein said neurological disease is selected from brain cancer, cancer metastasis to the brain, multiple sclerosis (MS), amyotrophic lateral sclerosis (ALS), Alzheimer's disease, Parkinson's disease, neurological injury, radiation induced injury to the brain, hypoxic injury to the brain and Rett syndrome.

4. The use of claim 3, wherein said brain cancer is any one of an astrocytic tumor, a glioma, a medulloblastoma, a neuroblastoma and a meningioma.

5. The use of claim 4, wherein said glioma is glioblastoma.

6. The use of claim 2, wherein said muscular disease is selected from MS, a muscular dystrophy, muscle injury, muscle inflammation, cachexia and sarcopenia.

7. The use of claim 6, wherein said muscular dystrophy is Duchenne's muscular dystrophy (DMD), or Baker muscular dystrophy.

8. The use of any one of claims 2, 6 or 7 wherein said disease is a muscle disease and wherein said extracellular vesicles, conditioned media, extracellular matrix or a

combination thereof comprise at least one of miR-29a, miR-29b, miR-29c and miR-656.

9. The use of claim 2, wherein said autoimmune disease is selected from MS, diabetes, colitis, and Chron's disease.

10. The use of claim 2, wherein said energy homeostasis disease is diabetes.

11. The use of claim 2, wherein said digestive disease is selected from irritable bowel syndrome (IBD), Chron's disease, and colitis.

12. The use of claim 2, wherein aging comprises at least one of skin aging, muscle aging, and brain aging.

13. The use of claim 2, wherein said proliferative disease is cancer.

14. The use of claim 13, wherein said cancer is any one of brain cancer, metastasis to the brain, lung cancer, breast cancer, colon cancer, pancreatic cancer, prostate cancer, and head and neck cancer.

15. The use of claim 14, wherein said brain cancer is selected from glioma, medulloblastoma, neuroblastoma and meningioma.

16. The use of claim 15, wherein said glioma is glioblastoma.

17. The use of any one of claims 13 to 16, wherein the subject is to be irradiated.

18. The use of any one of claims 13 to 17, wherein said MSC population, extracellular vesicles, conditioned media, extracellular matrix or a combination thereof comprise at least one of miR-145 and miR-656.

19. The use of any one of claims 1 to 18, wherein said enriched population of CH-MSCs is substantially devoid of amniotic placenta-derived MSCs (AM-MSCs).

20. The use of any one of claims 1 to 19, wherein the CH-MSCs are selected from a mix of cells or placental tissue.

21. The use of claim 20, wherein said selecting comprises selecting at least one cell expressing at least one surface marker selected from TCR alpha-beta, CD55, LIFR, ST6GALNACS, and MIC A/B.

22. The use of any one of claims 1 to 21, wherein the medicament is to be administered via at least one of intravenous administration, intramuscular administration, intranasal administration, intrathecal administration, intrastriatal administration, intracranial administration, intraarterial administration, and subcutaneous administration.

23. The use of any one of claims 1 to 22, wherein said CH-MSC population is allogenic to said subject.

24. The use of any one of claims 1 to 22, wherein said CH-MSC population is autologous to said subject.

25. The use of any one of claims 21 to 24 further comprising confirming expression of said at least one surface marker on the surface of said selected CH-MSC.

26. A method of selecting a mesenchymal stem cell (MSC) subpopulation, the method comprising:

(a) providing MSCs; and

(b) selecting at least one MSC expressing of at least one surface marker on said at least one MSC's surface, wherein expression of at least one of CD184, CD193, CD235a, CD318, CD255, CD268, fMLP, ITGA2, ITGA4, and CD326 indicates an MSC is an umbilical cord-derived MSC, expression of at least one of TCR alpha-beta, CD55, LIFR, ST6GALNACS, and MIC A/B indicates an MSC is a chorionic placenta-derived MSC, expression of at least one of CD24, CD48, CD66b, CD338, CD120b, CD268, FGFLR1, ITGA5, NES, and PDGFRAA indicates an MSC is a bone marrow-derived MSC, expression of at least one of CD84, PDGFRBB, and TNFRSF11B indicates an MSC is an adipose-derived MSC, and expression of CD157 indicates an MSC is an amniotic placenta-derived MSC;

thereby selecting an MSC subpopulation.

27. The method of claim 26, further comprising culturing the MSC in MSC growth media.

28. The method of claim 26 or 27, wherein said providing comprises providing tissue or a cell mixture and isolating MSCs from said tissue or cell mixture.

29. The method of claim 28, wherein said isolating MSCs comprises isolation of cells expressing a plurality of surface marker selected from CD9, CD10, CD13, CD26, CD29, CD44, CD36, CD46, CD47, CD49a, CD49b, CD49c, CD49d, CD49e, CD50, CD51/61, CD54, CD55, CD58, CD59, CD61, CD63, CD71, CD73, CD81, CD83, CD87, CD90, CD91, CD95, CD97, CD98, CD99, CD105, CD108, CD109, CD140b, CD142, CD146, CD147, CD151, CD164, CD165, CD166, CD273, β2-microglobulin, HLA-A,B,C, HLA-A2, and STRO1.

30. The method of claim 28 or 29, wherein said tissue is selected from placenta, umbilical cord, adipose tissue and bone marrow.

31. The method of any one of claims 26 to 30, further comprises confirming expression of said at least one surface marker on the surface of said selected MSC.

32. A pharmaceutical composition for use in treating a disease or condition comprising a pharmaceutically acceptable adjuvant, excipient or carrier and at least one of:

(a) an isolated and enriched population of CH-MSCs;

(b) extracellular vesicles derived from said CH-MSC population;

(c) conditioned media from said CH-MSC population; and

(d) extracellular matrix secreted by said CH-MSC population.

33. The pharmaceutical composition for use of claim 32, wherein said disease or condition is selected from a neurological disease, a muscular disease, an autoimmune disease, an inflammatory disease, a digestive disease, an energy homeostasis disease, aging, radiation induced injury, cell transplant rejection and a proliferative disease.

34. The pharmaceutical composition for use of claim 33, wherein said neurological disease is selected from brain cancer, cancer metastasis to the brain, multiple sclerosis (MS), amyotrophic lateral sclerosis (ALS), Alzheimer's disease, Parkinson's disease, neurological injury, radiation induced injury to the brain and Rett syndrome.

35. The pharmaceutical composition for use of claim 34, wherein said brain cancer is any one of a glioma, an astrocytic tumor, a medulloblastoma, neuroblastoma, and a meningioma.

36. The pharmaceutical composition for use of claim 35, wherein said glioma is glioblastoma.

37. The pharmaceutical composition for use of claim 33, wherein said muscular disease is selected from MS, a muscular dystrophy, muscle injury, muscle inflammation, cachexia and sarcopenia.

38. The pharmaceutical composition for use of claim 37, wherein said muscular dystrophy is Duchenne's muscular dystrophy (DMD).

39. The pharmaceutical composition for use of any one of claims 33, 37 or 38 wherein said disease is a muscle disease and wherein said extracellular vesicles, conditioned media or both comprise at least one of miR-29a, miR-29b, miR-29c and miR-656.

40. The pharmaceutical composition for use of claim 33, wherein said autoimmune disease is selected from MS, diabetes and Crohn's disease.

41. The pharmaceutical composition for use of claim 33, wherein said energy homeostasis disease is diabetes.

42. The pharmaceutical composition for use of claim 33, wherein said digestive disease is selected from irritable bowel syndrome (IBD), Chron's disease, and colitis.

43. The pharmaceutical composition for use of claim 33, wherein aging comprises skin aging.

44. The pharmaceutical composition for use of claim 33, wherein said proliferative disease is cancer.

45. The pharmaceutical composition for use of claim 44, wherein said cancer is any one of brain cancer, metastasis to the brain, lung cancer, breast cancer, colon cancer, pancreatic cancer, prostate cancer, and head and neck cancer.

46. The pharmaceutical composition for use of claim 45, wherein said brain cancer is selected from glioma, astrocytic tumors, medulloblastoma, neuroblastoma or meningioma.

47. The pharmaceutical composition for use of claim 46, wherein said glioma is glioblastoma.

48. The pharmaceutical composition for use of any one of claims 44 to 47, wherein the subject is to be irradiated.

49. The pharmaceutical composition for use of any one of claims 44 to 47, wherein said MSC population, extracellular vesicles, conditioned media or a combination thereof comprise at least one of miR-145 and miR-656.

50. The pharmaceutical composition for use of any one of claims 32 to 49, wherein said substantially pure population of CH-MSCs is substantially devoid of amniotic placenta-derived MSCs (AM-MSCs).

51. A method of maintaining stem cells and primary cells in culture, the method comprising,

(a) providing stem cells, primary cells or both;

(b) growing said stem cells, primary cells or both in culture medium comprising extracellular vesicles derived from MSCs,

thereby maintaining stem cells, primary cells or both in culture.

52. The method of claim 51, wherein said culture medium comprises conditioned media from said MSC.

53. The method of claim 51 or 52, wherein said culture medium comprises extracellular matrix from said MSC.

54. The method of any one of claims 51 to 53, wherein said growing comprises coculture of said stem cells, primary cells or both with said MSC.

55. The method of any one of claims 51 to 54, further comprising growing said stem cells, primary cells or both in primary cell growth media.

56. The method of any one of claims 51 to 54, wherein said maintaining comprises extending survival of said stem cells, primary cells or both beyond survival of said cells in culture medium substantially devoid of extracellular vesicles from said MSC.

57. The method of any one claims 51 to 56, wherein said maintaining comprises culturing said stem cells, primary cells or both in vitro for at least 10 passages.

58. The method of any one of claims 51 to 57, wherein said maintaining comprises said stem cells, primary cells or both retaining the ability to undergo both symmetric and asymmetric divisions.

59. The method of any one of claims 51 to 58, wherein said MSCs are umbilical cord-derived MSCs (UC-MSCs), CH-MSCs or a combination thereof.

60. The method of claim 59, wherein said MSCs are CH-MSCs.

61. The method of any one of claims 51 to 58, wherein said stem cell are cancer stem cells and said MSCs are bone marrow-derived MSCs, (BM-MSCs), adipose-derived MSCs (AD-MSCs), AM-MSCs, or a combination thereof.

62. A pharmaceutical composition comprising at least one of: a mesenchymal stem cell (MSC) population, extracellular vesicles secreted from said MSC population, conditioned media from said MSC population and a combination thereof; said MSC population is characterized by an expression profile selected from any one of Tables 1-5.

63. The pharmaceutical composition of claim 62, further comprising a pharmaceutically acceptable carrier.