remyelination (11), regeneration is ascribed directly to transfer of hematopoietic cells from the younger parabiont.

[0005] Despite these benefits, parabiont pairings, that is, the sharing of circulations between a younger and an older animal, is not practical due to ABO blood group incompatibilities. Parabiosis is also complicated by parabiotic intoxication, a form of runting disease or graft versus host disease (3), due to the immune cells of the younger animal attacking the organs of the older parabiont.

SUMMARY

[0006] The methods described herein are based on the discovery that nonviable pluripotent stem cells can be used to for transbiosis (heterochronic cellular transplantation) to improve age-related declines in tissue and organ function, including, for example, improving cognition, slowing the progression of age-related cognitive impairment, and improving age-related cardiac impairment.

[0006a] In one aspect, the present disclosure refers to the use of a composition comprising an amount of lyophilized nonviable pluripotent stem cells effective to improve cognition in a subject in need thereof in the manufacture of a medicament for treating one or more symptoms of cognitive impairment in the subject, wherein the medicament is formulated for at least one of topical, enteral, subcutaneous, intraperitoneal, intramuscular, and intravascular administration, and wherein at least a portion of the intact cell membranes is preserved in the lyophilized nonviable pluripotent stem cells.

[0006b] In another aspect, the present disclosure refers to the use of a composition comprising an amount of lyophilized nonviable pluripotent stem cells effective to slow the progression of cognitive impairment in a subject in the manufacture of a medicament for slowing the progression of cognitive impairment in the subject with age-related cognitive impairment, wherein the medicament is formulated for at least one of topical, enteral, subcutaneous, intraperitoneal, intramuscular, and intravascular administration, and wherein at least a portion of the intact cell membranes is preserved in the lyophilized nonviable pluripotent stem cells.

[0007] As described herein, nonviable pluripotent stem cells are administered to a subject in need of treatment therewith to provide a physiologically younger phenotype and function to an organ or tissue by the transplantation of the nonviable pluripotent stem cells.

[0008] In one approach, a method is provided for improving cognition in a subject in need thereof, the method comprising administering a composition comprising an amount of nonviable pluripotent stem cells effective to improve cognition in the subject.

[0009] In another approach, a method is provided for slowing the progression of cognitive impairment in a subject with age-related cognitive impairment, the method comprising administering a composition comprising an amount of nonviable pluripotent stem cells effective to slow the progression of cognitive impairment in the subject.

[0010] In yet another approach, a method is provided for improving age-related organ or tissue dysfunction in a subject in need thereof, the method comprising administering a composition comprising an amount of nonviable pluripotent stem cells effective to improve age-related organ or tissue dysfunction in the subject.

[0011] The term "effective amount," "therapeutically effective amount," or similar phrase means the amount that will elicit the biological or medical response of a subject that is being sought by a medical doctor or other clinician. In one example, the term "effective amount" is intended to mean the amount that will bring about a biologically meaningful improvement in the treated subject. Successful treatment using the methods described herein can be determined by a skilled clinician based upon routine clinical practice.

[0012] The pluripotent stem cells useful herein are nonviable. Nonviable pluripotent stem cells, including pluripotent stem cells that have been lethally irradiated or lyophilized into a powder, remain capable of improving age-related declines in tissue and organ function, as well as repairing damaged organs or tissues in a subject. No adverse effects have been noted after treatment. At least in some approaches, it has been found that lyophilized pluripotent stem cells have better efficacy than lethally irradiated pluripotent stem cells.

[0013] The pluripotent stem cells useful herein can include pluripotent stem cells from all sources, such as but not limited to embryo, placenta, amniotic fluid, bone marrow, or those derived *ex vivo* from adult stem cells or adult somatic cells, and specifically includes embryonic

stem cells (ESCs), modified adult stem or somatic cells (ASCs), that is, induced pluripotent stem cells (iPSC), and very small embryonic-like stem cells (VSELs).

BRIEF DESCRIPTION OF THE DRAWINGS

[0014] FIG. 1 is a microscopic picture of a lyophilized embryonic stem cell in trehelose matrix wherein the ESC is nonviable and fixed in a freeze-dried (lyophilized) state.

[0015] FIG. 2 is a bar graph showing the total percent of tests failed by aged (18 month old) mice on training day in a Morris Water Maze Test. Aged mice were treated with intraperitoneal (IP) injection of normal saline (NS; control), IP injection of irradiated embryonic stem cells (ESC) in NS, or IP injection of lyophilized ESC in NS.

[0016] FIG. 3 is a line graph showing the training day improvement in time (in seconds) to the escape platform of aged (18 month old) mice in a Morris Water Maze test. Mice were treated with either intraperitoneal (IP) injection of normal saline (NS) or IP injection of lyophilized ESC dissolved in NS.

[0017] FIG. 4 is a bar graph showing the results of a long-term memory test of aged (18 month old) mice in the Morris Water Maze test. Mice were treated with either intraperitoneal (IP) injection of normal saline (NS) or IP injection of lyophilized ESC dissolved in NS.

CLAIMS

What is claimed is:

1. Use of a composition comprising an amount of lyophilized nonviable pluripotent stem cells effective to improve cognition in a subject in need thereof in the manufacture of a medicament for treating one or more symptoms of cognitive impairment in the subject, wherein the medicament is formulated for at least one of topical, enteral, subcutaneous, intraperitoneal, intramuscular, and intravascular administration, and wherein at least a portion of the intact cell membranes is preserved in the lyophilized nonviable pluripotent stem cells.

2. The use according to claim 1, further comprising that the composition is to be prepared by mixing nonviable pluripotent stem cells with liquid media.

3. The use according to claim 2, wherein the liquid media comprises saline.

4. The use according to any one of claims 1 to 3, wherein the subject is a human.

5. The use according to claim 4, wherein the human subject is in need of treatment for a deficiency in at least one of the following cognitive abilities: reasoning, judgment, perception, attention, memory, motor skills, language, coordination, intelligence, and visual and spatial processing.

6. The use according to any one of claims 1 to 5, wherein the pluripotent stem cells do not include conditioned media.

7. The use according to any one of claims 1 to 6, wherein the pluripotent stem cells are embryonic stem cells.

8. The use according to any one of claims 1 to 7, wherein improving cognition includes improving memory.

9. Use of a composition comprising an amount of lyophilized nonviable pluripotent stem cells effective to slow the progression of cognitive impairment in a subject in the manufacture of a medicament for slowing the progression of cognitive impairment in the subject with age-related cognitive impairment, wherein the medicament is formulated for at least one of topical, enteral,

subcutaneous, intraperitoneal, intramuscular, and intravascular administration, and wherein at least a portion of the intact cell membranes is preserved in the lyophilized nonviable pluripotent stem cells.

10. The use according to claim 9, further comprising that the composition is to be prepared by mixing nonviable pluripotent stem cells with liquid media.

11. The use according to claim 10, wherein the liquid media comprises saline.

12. The use according to any one of claims 9 to 11, wherein the subject is a human.

13. The use according to any one of claims 9 to 12, wherein the pluripotent stem cells do not include conditioned media.

14. The use according to any one of claims 9 to 13, wherein the pluripotent stem cells are embryonic stem cells.

15. The use according to any one of claims 9 to 14, wherein the cognitive impairment is a deficiency in at least one of the following: reasoning, judgment, perception, attention, memory, motor skills, language, coordination, intelligence, and visual and spatial processing.