

WHAT IS CLAIMED IS:

1. A method of treating non-ischemic dilated cardiomyopathy in a subject, comprising administering a therapeutically effective amount of a population of isolated allogeneic human mesenchymal stem cells to a subject in need thereof, wherein the number of exhausted B cells (CD19⁺, CD27⁻, IgD⁻) in a sample of the subject's serum decreases by at least 25% as compared to the number of exhausted B cells in a sample of the subject's serum prior to administration of said population of isolated allogeneic human mesenchymal stem cells, thereby treating said non-ischemic dilated cardiomyopathy.
2. A method of treating non-ischemic dilated cardiomyopathy in a subject, comprising administering a therapeutically effective amount of a population of isolated allogeneic human mesenchymal stem cells to a subject in need thereof, wherein the number of switched memory B cells (CD19⁺, CD27^{high}, IgD⁻) in a sample of the subject's serum increases by at least 100% as compared to the number of switched memory B cells in a sample of the subject's serum prior to administration of said population of isolated allogeneic human mesenchymal stem cells, thereby treating said non-ischemic dilated cardiomyopathy.
3. A method of treating non-ischemic dilated cardiomyopathy in a subject, comprising administering a therapeutically effective amount of a population of isolated allogeneic human mesenchymal stem cells to a subject in need thereof, wherein the number of B-cells expressing intracellular TNF- α in a sample of the subject's serum decreases by at least 30% as compared to the number of B-cells expressing intracellular TNF- α in a sample of the subject's serum prior to administration of said population of isolated allogeneic human mesenchymal stem cells, thereby treating said non-ischemic dilated cardiomyopathy.
4. A method of treating non-ischemic dilated cardiomyopathy in a subject, comprising administering a therapeutically effective amount of a population of isolated allogeneic human mesenchymal stem cells to a subject in need thereof, wherein the number of early activated T-cells (CD3⁺, CD69⁺) in a sample of the subject's serum decreases by at least 30% as compared to the number of early activated T-cells in a sample of the subject's serum prior to administration of said population of isolated allogeneic human mesenchymal stem cells, thereby treating said non-ischemic dilated cardiomyopathy.
5. A method of treating non-ischemic dilated cardiomyopathy in a subject, comprising administering a therapeutically effective amount of a population of isolated allogeneic human mesenchymal stem cells to a subject in need thereof, wherein the number of chronic activated T-cells (CD3⁺, CD25⁺) in a sample of the subject's serum decreases by at least 70% as

compared to the number of chronic activated T-Cells in a sample of the subject's serum prior to administration of said population of isolated allogeneic human mesenchymal stem cells, thereby treating said non-ischemic dilated cardiomyopathy.

6. A method of treating non-ischemic dilated cardiomyopathy in a subject, comprising administering a therapeutically effective amount of a population of isolated allogeneic human mesenchymal stem cells to a subject in need thereof, wherein the number of Temra cells (CD45RA⁺, CCR7⁻) in a sample of the subject's serum decreases by at least 40% as compared to the number of Temra cells in a sample of the subject's serum prior to administration of said population of isolated allogeneic human mesenchymal stem cells, thereby treating said non-ischemic dilated cardiomyopathy.

7. A method of treating non-ischemic dilated cardiomyopathy in a subject, comprising administering a therapeutically effective amount of a population of isolated allogeneic human mesenchymal stem cells to a subject in need thereof, wherein the TNF- α concentration in a sample of the subject's serum decreases by at least 80% as compared to the TNF- α concentration in a sample of the subject's serum prior to administration of said population of isolated allogeneic human mesenchymal stem cells, thereby treating said non-ischemic dilated cardiomyopathy.

8. A method of treating symptoms of aging frailty in a subject, comprising administering a therapeutically effective amount of a population of isolated allogeneic human mesenchymal stem cells to a subject in need thereof, wherein the number of exhausted B cells (CD19⁺, CD27⁻, IgD⁻) in a sample of the subject's serum decreases by at least 10% as compared to the number of exhausted B cells in a sample of the subject's serum prior to administration of said population of isolated allogeneic human mesenchymal stem cells, thereby treating said symptoms of aging frailty.

9. A method of treating symptoms of aging frailty in a subject, comprising administering a therapeutically effective amount of a population of isolated allogeneic human mesenchymal stem cells to a subject in need thereof, wherein the number of switched memory B cells (CD19⁺, CD27^{high}, IgD⁻) in a sample of the subject's serum increases by at least 75% as compared to the number of switched memory B cells in a sample of the subject's serum prior to administration of said population of isolated allogeneic human mesenchymal stem cells, thereby treating said symptoms of aging frailty.

10. A method of treating symptoms of aging frailty in a subject, comprising administering a therapeutically effective amount of a population of isolated allogeneic human mesenchymal

stem cells to a subject in need thereof, wherein the number of B-cells expressing intracellular TNF- α in a sample of the subject's serum decreases by at least 60% as compared to the number of B-cells expressing intracellular TNF- α in a sample of the subject's serum prior to administration of said population of isolated allogeneic human mesenchymal stem cells, thereby treating said symptoms of aging frailty.

11. A method of treating symptoms of aging frailty in a subject, comprising administering a therapeutically effective amount of a population of isolated allogeneic human mesenchymal stem cells to a subject in need thereof, wherein the number of early activated T-cells (CD3⁺, CD69⁺) in a sample of the subject's serum decreases by at least 30% as compared to the number of early activated T-cells in a sample of the subject's serum prior to administration of said population of isolated allogeneic human mesenchymal stem cells, thereby treating said symptoms of aging frailty.

12. A method of treating symptoms of aging frailty in a subject, comprising administering a therapeutically effective amount of a population of isolated allogeneic human mesenchymal stem cells to a subject in need thereof, wherein the number of chronic activated T-cells (CD3⁺, CD25⁺) in a sample of the subject's serum decreases by at least 75% as compared to the number of chronic activated T-Cells in a sample of the subject's serum prior to administration of said population of isolated allogeneic human mesenchymal stem cells, thereby treating said symptoms of aging frailty.

13. A method of treating symptoms of aging frailty in a subject, comprising administering a therapeutically effective amount of a population of isolated allogeneic human mesenchymal stem cells to a subject in need thereof, wherein the number of Temra cells (CD45RA⁺, CCR7⁻) in a sample of the subject's serum decreases by at least 20% as compared to the number of Temra cells in a sample of the subject's serum prior to administration of said population of isolated allogeneic human mesenchymal stem cells, thereby treating said symptoms of aging frailty.

14. A method of treating symptoms of aging frailty in a subject, comprising administering a therapeutically effective amount of a population of isolated allogeneic human mesenchymal stem cells to a subject in need thereof, wherein the TNF- α concentration in a sample of the subject's serum decreases by at least 50% as compared to the TNF- α concentration in a sample of the subject's serum prior to administration of said population of isolated allogeneic human mesenchymal stem cells, thereby treating said symptoms of aging frailty.

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15. A method of treating symptoms of aging frailty in a subject, comprising administering a therapeutically effective amount of a population of isolated allogeneic human mesenchymal stem cells to a subject in need thereof, wherein the CD4⁺:CD8⁺ T cell ratio in a sample of the subject's serum increases by at least 100% as compared to the CD4⁺:CD8⁺ T cell ratio in a sample of the subject's serum prior to administration of said population of isolated allogeneic human mesenchymal stem cells, thereby treating said symptoms of aging frailty.
16. The method of any one of claims 1-7, wherein the subject is a human.
17. The method of any one of claims 8-15, wherein the subject exhibits inflammaging.
18. The method of any one of claims 1-17, wherein the mesenchymal stem cells are bone marrow-derived mesenchymal stem cells.
19. The method of any one of claims 1-18, wherein the mesenchymal stem cells do not express STRO-1.
20. The method of any one of claims 1-8, wherein the mesenchymal stem cells do not express CD45.
21. The method of any one of claims 1-20, wherein the mesenchymal stem cells do not express fibroblast surface markers or have a fibroblast morphology.
22. The method of any one of claims 1-21, wherein the mesenchymal stem cells are not genetically manipulated.
23. The method of any one of claims 1-22, wherein the isolated population of allogeneic mesenchymal stem cells is administered in a single dose.
24. The method of any one of claims 1-22, wherein the isolated population of allogeneic mesenchymal stem cells is administered in two or more doses.
25. The method of any one of claims 1-22, wherein the isolated population of allogeneic mesenchymal stem cells is administered at least yearly.
26. The method of any one of claims 1-25, wherein the isolated population of allogeneic mesenchymal stem cells is administered systemically.
27. The method of any one of claims 1-26, wherein the isolated population of allogeneic mesenchymal stem cells is administered by infusion or direct injection.
28. The method of any one of claims 1-27, wherein the isolated population of allogeneic mesenchymal stem cells is administered intravenously, intraarterially, or intraperitoneally.
29. The method of claim 28, wherein the isolated population of allogeneic mesenchymal stem cells is administered intravenously.

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30. The method of any one of claims 1-25, wherein the isolated population of allogeneic mesenchymal stem cells is administered intramuscularly, intravenously, intraarterially, intraperitoneally, subcutaneously, intradermally, orally, tranendocardially, or intranasally.
31. The method of claim 30, wherein the isolated population of allogeneic mesenchymal stem cells is administered intramuscularly.
32. The method of any one of claims 1-31, wherein the isolated population of allogeneic mesenchymal stem cells is administered at a dose of about 20×10^6 mesenchymal stem cells.
33. The method of any one of claims 1-31, wherein the isolated population of allogeneic mesenchymal stem cells is administered at a dose of about 100×10^6 mesenchymal stem cells.
34. The method of any one of claims 1-31, wherein the isolated population of allogeneic mesenchymal stem cells is administered at a dose of about 200×10^6 mesenchymal stem cells.
35. The method of any one of claims 1-34, wherein the isolated population of allogeneic mesenchymal stem cells are obtained from a human donor and wherein a step of MHC matching of the human donor to the subject is not employed prior to the administration of the isolated population of allogeneic mesenchymal stem cells to the subject.
36. A method of evaluating cellular and humoral immunity status in a subject, comprising:
- (1) obtaining a serum sample from a subject selected for evaluation based on a determination that the subject was previously in need of treatment of non-ischemic dilated cardiomyopathy and said subject had been administered an initial dose of an isolated population of allogeneic human mesenchymal stem cells;
 - (2) performing one or more assays configured to detect a non-ischemic dilated cardiomyopathy marker selected from the group of exhausted B cells ($CD19^+$, $CD27^-$, IgD^-), switched memory B cells ($CD19^+$, $CD27^{high}$, IgD^-), B-cells expressing intracellular $TNF-\alpha$, early activated T-cells ($CD3^+$, $CD69^+$), chronic activated T-cells ($CD3^+$, $CD25^+$), Temra cells ($CD45RA^+$, $CCR7^-$), and serum $TNF-\alpha$ by introducing the serum sample obtained from the subject into an assay instrument which (i) contacts the serum sample with one or more antibodies which specifically bind for detection the biomarker(s) which are assayed, and (ii) generates one or more assay results indicating of binding of each biomarker which is assayed to a respective antibody to provide one or more assay results;
 - (3) correlating the assay result(s) generated by the assay instrument to the immunity status of the subject, wherein said correlating step comprises assigning a likelihood of one or more future changes in immune status to the subject based on the assay result(s); and

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(4) treating the subject based on the predetermined subpopulation of individuals to which the subject is assigned, wherein the treatment comprises administration of one or more additional doses of an isolated population of allogeneic human mesenchymal stem cells.

37. A method of evaluating cellular and humoral immunity status in a subject, comprising:

(1) obtaining a serum sample from a subject selected for evaluation based on a determination that the subject was previously in need of treatment of symptoms of aging frailty and said subject had been administered an initial dose of an isolated population of allogeneic human mesenchymal stem cells;

(2) performing one or more assays configured to detect aging frailty marker selected from the group of exhausted B cells (CD19⁺, CD27⁻, IgD⁻), switched memory B cells (CD19⁺, CD27^{high}, IgD⁻), B-cells expressing intracellular TNF- α , early activated T-cells (CD3⁺, CD69⁺), chronic activated T-cells (CD3⁺, CD25⁺), Temra cells (CD45RA⁺, CCR7⁻), the CD4⁺:CD8⁺ T cell ratio, and serum TNF- α by introducing the serum sample obtained from the subject into an assay instrument which (i) contacts the serum sample with one or more antibodies which specifically bind for detection the biomarker(s) which are assayed, and (ii) generates one or more assay results indicating of binding of each biomarker which is assayed to a respective antibody to provide one or more assay results;

(3) correlating the assay result(s) generated by the assay instrument to the immunity status of the subject, wherein said correlating step comprises assigning a likelihood of one or more future changes in immune status to the subject based on the assay result(s); and

(4) treating the subject based on the predetermined subpopulation of individuals to which the subject is assigned, wherein the treatment comprises administration of one or more additional doses of an isolated population of allogeneic human mesenchymal stem cells.

38. The method of claims 36 or 37, wherein said one or more future changes in immune status comprise one or more of an increase in the number of exhausted B cells (CD19⁺, CD27⁻, IgD⁻), a decrease in the number of switched memory B cells (CD19⁺, CD27^{high}, IgD⁻), an increase in the number of B-cells expressing intracellular TNF- α , an increase in the number of early activated T-cells (CD3⁺, CD69⁺), an increase in the number of chronic activated T-cells (CD3⁺, CD25⁺), an increase in the number of Temra cells (CD45RA⁺, CCR7⁻), a decrease in the CD4⁺:CD8⁺ T cell ratio, and an increase in serum TNF- α .

39. An *in vitro* method of determining efficacy of treatment of non-ischemic dilated cardiomyopathy in a subject comprising: determining the levels of one or more biomarkers selected from the group consisting of exhausted B cells (CD19⁺, CD27⁺, IgD⁻), switched memory B cells (CD19⁺, CD27^{high}, IgD⁻), B-cells expressing intracellular TNF- α , early activated T-cells (CD3⁺, CD69⁺), chronic activated T-cells (CD3⁺, CD25⁺), Temra cells (CD45RA⁺, CCR7⁻), and the TNF- α concentration in serum obtained from the subject before and after administration of a population of isolated allogeneic human mesenchymal stem cells to the subject, and comparing the levels of the one or more biomarkers in the serum obtained before and after administration of the population of isolated human mesenchymal stem cells, wherein treatment is efficacious if

(1) the number of exhausted B cells (CD19⁺, CD27⁺, IgD⁻) decreases by at least 25% as compared to the number of exhausted B cells prior to administration of said population of isolated allogeneic human mesenchymal stem cells,

(2) the number of switched memory B cells (CD19⁺, CD27^{high}, IgD⁻) increases by at least 100% as compared to the number of switched memory B cells prior to administration of said population of isolated allogeneic human mesenchymal stem cells,

(3) the number of B-cells expressing intracellular TNF- α decreases by at least 30% as compared to the number of B-cells expressing intracellular TNF- α prior to administration of said population of isolated allogeneic human mesenchymal stem cells,

(4) the number of early activated T-cells (CD3⁺, CD69⁺) decreases by at least 30% as compared to the number of early activated T-cells prior to administration of said population of isolated allogeneic human mesenchymal stem cells,

(5) the number of chronic activated T-cells (CD3⁺, CD25⁺) decreases by at least 70% as compared to the number of chronic activated T-Cells prior to administration of said population of isolated allogeneic human mesenchymal stem cells,

(6) the number of Temra cells (CD45RA⁺, CCR7⁻) decreases by at least 40% as compared to the number of Temra cells prior to administration of said population of isolated allogeneic human mesenchymal stem cells, and/or

(7) the TNF- α concentration in a sample of the subject's serum decreases by at least 80% as compared to the TNF- α concentration in a sample of the subject's serum prior to administration of said population of isolated allogeneic human mesenchymal stem cells.

40. An *in vitro* method of determining efficacy of treatment of symptoms of aging frailty in a subject comprising: determining the levels of one or more biomarkers selected from the

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group consisting of exhausted B cells ($CD19^+$, $CD27^-$, IgD^-), switched memory B cells ($CD19^+$, $CD27^{high}$, IgD^-), B-cells expressing intracellular $TNF-\alpha$, early activated T-cells ($CD3^+$, $CD69^+$), chronic activated T-cells ($CD3^+$, $CD25^+$), Temra cells ($CD45RA^+$, $CCR7^-$), the $CD4^+$: $CD8^+$ T cell ratio, and the $TNF-\alpha$ concentration in serum obtained from the subject before and after administration of a population of isolated allogeneic human mesenchymal stem cells to the subject, and comparing the levels of the one or more biomarkers in the serum obtained before and after administration of the population of isolated human mesenchymal stem cells, wherein treatment is efficacious if

(1) the number of exhausted B cells ($CD19^+$, $CD27^-$, IgD^-) decreases by at least 10% as compared to the number of exhausted B cells prior to administration of said population of isolated allogeneic human mesenchymal stem cells,

(2) the number of switched memory B cells ($CD19^+$, $CD27^{high}$, IgD^-) increases by at least 75% as compared to the number of switched memory B cells prior to administration of said population of isolated allogeneic human mesenchymal stem cells,

(3) the number of B-cells expressing intracellular $TNF-\alpha$ decreases by at least 60% as compared to the number of B-cells expressing intracellular $TNF-\alpha$ prior to administration of said population of isolated allogeneic human mesenchymal stem cells,

(4) the number of early activated T-cells ($CD3^+$, $CD69^+$) decreases by at least 30% as compared to the number of early activated T-cells prior to administration of said population of isolated allogeneic human mesenchymal stem cells,

(5) the number of chronic activated T-cells ($CD3^+$, $CD25^+$) decreases by at least 75% as compared to the number of chronic activated T-Cells prior to administration of said population of isolated allogeneic human mesenchymal stem cells,

(6) the number of Temra cells ($CD45RA^+$, $CCR7^-$) decreases by at least 20% as compared to the number of Temra cells prior to administration of said population of isolated allogeneic human mesenchymal stem cells,

(7) the $TNF-\alpha$ concentration in a sample of the subject's serum decreases by at least 50% as compared to the $TNF-\alpha$ concentration in a sample of the subject's serum prior to administration of said population of isolated allogeneic human mesenchymal stem cells, and/or

(8) the $CD4^+$: $CD8^+$ T cell ratio in a sample of the subject's serum increases by at least 100% as compared to the $CD4^+$: $CD8^+$ T cell ratio in a sample of the subject's serum

prior to administration of said population of isolated allogeneic human mesenchymal stem cells.

41. Use *in vitro* of the levels of exhausted B cells (CD19⁺, CD27⁻, IgD⁻), the levels of switched memory B cells (CD19⁺, CD27^{high}, IgD⁻), the levels of B-cells expressing intracellular TNF- α , the levels of early activated T-cells (CD3⁺, CD69⁺), the levels of chronic activated T-cells (CD3⁺, CD25⁺), the levels of Temra cells (CD45RA⁺, CCR7⁻), and the TNF- α concentration in serum for determining whether treatment for non-ischemic dilated cardiomyopathy is efficacious.

42. Use *in vitro* of the levels of exhausted B cells (CD19⁺, CD27⁻, IgD⁻), the levels of switched memory B cells (CD19⁺, CD27^{high}, IgD⁻), the levels of B-cells expressing intracellular TNF- α , the levels of early activated T-cells (CD3⁺, CD69⁺), the levels of chronic activated T-cells (CD3⁺, CD25⁺), the levels of Temra cells (CD45RA⁺, CCR7⁻), the CD4⁺:CD8⁺ T cell ratio, and the TNF- α concentration in serum for determining whether treatment for aging frailty is efficacious.