CLAIMS

What is claimed is:

1. A method of producing an MSC population with enhanced regenerative potential, comprising:

a) culturing an MSC-containing population of cells in a culture medium to a confluence of 80% to 90% over each of at least four population doublings to provide a population enriched in large-MSC cells, wherein the four population doublings are measured from initial extraction of the MSC-containing population from a source; and

b) biophysically sorting the MSC-containing population of cells produced in (a) and collecting a large-MSC population of cells from the MSC-containing population, thereby producing an MSC population with enhanced regenerative potential.

2. The method of claim 1, wherein the biophysical sorting of the MSC-containing population comprises applying the MSC-containing population of cells to an inlet of an MSC-dimensioned microfluidic device and collecting a large-MSC population of cells from an outlet of the MSC-dimensioned microfluidic device.

3. The method of claim 1, further comprising culturing the large-MSC population.

4. The method of claim 3, comprising collecting conditioned medium from the large-MSC culture.

5. The method of claim 4, wherein the large-MSC culture medium contains increased amounts of one or more of IL-6, IL-8, MCP-1, EGF, VEGF, FGF1, FGF2, BMP2, ANG1, osteopontin, Igfbp2, Angptl2, Angptl3, and Angptl5 compared to a culture medium obtained from small-MSCs.

6. The method of claim 1, further comprising collecting a small-MSC population from an outlet of the MSC-dimensioned microfluidic device.

7. The method of claim 6, further comprising culturing the small-MSC population.

8. The method of claim 7, comprising applying the cultured small-MSC population to an inlet of an MSC-dimensioned microfluidic device and collecting a large-MSC population from an outlet of the MSC-dimensioned microfluidic device.

9. The method of claim 1, wherein the MSC-containing population of cells is obtained from bone marrow, is a cultured MSC-containing population of cells or an uncultured MSC-containing population of cells.

10. The method of claim 1, further comprising trypsinizing the MSC-containing population of cells after the MSC-containing population of cells has been cultured to a confluence of 80% to 90%.

11. The method of claim 10, wherein trypsinizing is performed after each of the at least four population doublings.

12. The method of claim 10, further comprising cryopreserving a portion of the MSC-containing population of cells in a cryopreservation medium after trypsinization, after about 4 to about 6 population doublings or after about 12 population doublings.

13. The method of claim 1, wherein the biophysical sorting has a throughput of at least about 10^3 cells/minute, or about 1-5 x 10^6 cells/minute.

14. A method of culturing an MSC-containing population cells to produce an MSC population with enhanced regenerative potential, comprising:

a) culturing an MSC-containing population of cells in a culture medium to a confluence of 80% to 90%;

b) optionally trypsinizing the MSC-containing population of cells;

c) repeating a) and b) so that the MSC-containing population of cells doubles at least four times, as measured from initial extraction of the MSC-containing population from a source, to thereby produce an MSC population with enhanced regenerative potential; and

d) optionally cryopreserving a portion of the MSC-containing population of cells in a cryopreservation medium after one or more population doublings.

15. The method of claim 14, wherein the MSC-containing population of cells is obtained from bone marrow.

16. The method of claim 14, wherein a portion of the MSC-containing population of cells is cryopreserved after about four to six population doublings.

17. The method of claim 16, wherein a portion of the MSC-containing population of cells is cryopreserved after about twelve population doublings.

18. The method of claim 16, wherein the cryopreservation medium comprises Dulbecco's Modified Eagle's Medium, fetal bovine serum, and dimethyl sulfoxide.

19. The method of claim 16, wherein the cryopreservation medium consists essentially of 70% Dulbecco's Modified Eagle's Medium Low Glucose, 20% fetal bovine serum, and 10% dimethyl sulfoxide.

20. A method of producing an MSC population with enhanced regenerative potential, comprising:

a) culturing an MSC-containing population of cells in a culture medium to a confluence of 80% to 90% over each of at least four population doublings to provide a population enriched in large-MSC cells, wherein the four population doublings are measured from initial extraction of the MSC-containing population from a source, wherein the MSC-containing population of cells are seeded, initially and at subsequent passages, at about 1000 MSC/cm^2 to 1500 MSC/cm^2; and

b) biophysically sorting the MSC-containing population of cells produced in (a) and collecting a large-MSC population of cells from the MSC-containing

population, thereby producing an MSC population with enhanced regenerative potential.