CLAIMS

1. A composition for regeneration of an intervertebral disc, comprising a monovalent metal salt of alginic acid and mesenchymal stem cells.

2. The composition according to claim 1, wherein the mesenchymal stem cells are human bone marrow-derived high-purity mesenchymal stem cells.

3. The composition according to claim 2, wherein the human bone marrow-derived high-purity mesenchymal stem cells are a cell population of LNGFR (CD271)-positive, or LNGFR (CD271) and Thy-1 (CD90) double-positive, rapidly proliferating mesenchymal stem cell clones, said cell population satisfying at least one of the following characteristics (a) and (b):

(a) the coefficient of variation of forward scattered light in flow cytometry is 40% or less; and

(b) the average cell size is 20 μm or less.

4. The composition according to claim 2 or 3, wherein the human bone marrow-derived high-purity mesenchymal stem cells are a cell population of rapidly proliferating mesenchymal stem cell clones that are separated using, as an indicator, the feature that the cells are LNGFR (CD271)-positive, or LNGFR (CD271) and Thy-1 (CD90) double-positive cells, said cell population satisfying at least one of the following characteristics (a) and (b):

(a) the coefficient of variation of forward scattered light in flow cytometry is 40% or less; and

(b) the average cell size is 20 μm or less.

5. The composition according to any one of claims 1 to 4, wherein the monovalent metal salt of alginic acid is a low endotoxin monovalent metal salt of alginic acid.

6. The composition according to any one of claims 1 to 5, wherein the monovalent metal salt of alginic acid has a weight average molecular weight (absolute molecular weight) of 80,000 or more, as measured by a GPC-MALS method.

7. The composition according to any one of claims 1 to 6, wherein the concentration of the monovalent metal salt of alginic acid is 0.5 w/w% to 5.0 w/w%.

8. The composition according to any one of claims 1 to 7 for use in regeneration of the intervertebral disc, wherein regeneration of a nucleus pulposus of the intervertebral disc is promoted via activation of nucleus pulposus cells by the mesenchymal stem cells and/or differentiation of the mesenchymal stem cells into the nucleus pulposus cells.

9. The composition for use according to claim 8, wherein the composition is to be applied to the intervertebral disc of a subject and, after the application thereof, a crosslinking agent is to be brought into contact with at least a part of a surface of the composition, and wherein the composition has fluidity upon the application thereof.

10. The composition for use according to claim 9, wherein the composition is to be applied to a nucleus pulposus site of the intervertebral disc.

11. The composition for use according to claim 10, wherein application of the composition to the nucleus pulposus site comprises filling of the composition into a defective site of the nucleus pulposus.

12. The composition for use according to any one of claims 9 to 11, wherein the crosslinking agent is a divalent or higher valent metal ion compound.

13. The composition for use according to any one of claims 8 to 12, wherein the use is in treatment, prevention or recurrence suppression of intervertebral disc degeneration and/or intervertebral disc damage.

14. The composition for use according to claim 13, wherein the intervertebral disc degeneration and/or the intervertebral disc damage are at least one selected from the group consisting of intervertebral disc herniation, discopathy, degenerative spondylolisthesis, pyogenic discitis, spondylosis deformans, spinal canal stenosis, and intervertebral disc damage.

15. A composition for use in regeneration of an intervertebral disc, comprising a monovalent metal salt of alginic acid and human bone marrow-derived high-purity mesenchymal stem cells, wherein the composition is to be applied to a nucleus pulposus site of the intervertebral disc of a subject in a state in which the composition has fluidity.

16. The composition for use according to claim 15, wherein the composition is to be then used without bringing a crosslinking agent into contact with the composition.

17. The composition for use according to claim 15 or 16, wherein regeneration of a nucleus pulposus of the intervertebral disc is promoted via activation of nucleus pulposus cells by the human bone marrow-derived high-purity mesenchymal stem cells and/or differentiation of the human bone marrow-derived high-purity mesenchymal stem cells into the nucleus pulposus cells.

18. The composition for use according to any one of claims 15 to 17, wherein the human bone marrow-derived high-purity mesenchymal stem cells are in an undifferentiated state upon the application thereof and/or are to be applied without treatments of induction of differentiation.

19. The composition for use according to any one of claims 15 to 18, wherein the human bone marrow-derived high-purity mesenchymal stem cells are a cell population of LNGFR (CD271)-positive, or LNGFR (CD271) and Thy-1 (CD90) double-positive, rapidly proliferating mesenchymal stem cell clones, said cell population satisfying at least one of the following characteristics (a) and (b):

(a) the coefficient of variation of forward scattered light in flow cytometry is 40% or less; and

(b) the average cell size is 20 μm or less.

20. The composition for use according to any one of claims 15 to 19, wherein the human bone marrow-derived high-purity mesenchymal stem cells are a cell population of rapidly proliferating mesenchymal stem cell clones that are separated using, as an indicator, the feature that the cells are LNGFR (CD271)-positive, or

LNGFR (CD271) and Thy-1 (CD90) double-positive cells, said cell population satisfying at least one of the following characteristics (a) and (b):

(a) the coefficient of variation of forward scattered light in flow cytometry is 40% or less; and

(b) the average cell size is 20 μm or less.

21. The composition for use according to any one of claims 15 to 20, wherein the monovalent metal salt of alginic acid is a low endotoxin monovalent metal salt of alginic acid.

22. The composition for use according to any one of claims 15 to 21, wherein the monovalent metal salt of alginic acid has a weight average molecular weight (absolute molecular weight) of 80,000 or more, as measured by a GPC-MALS method.

23. The composition for use according to any one of claims 15 to 22, wherein the concentration of the monovalent metal salt of alginic acid is 0.5 w/w% to 5.0 w/w%.

24. The composition for use according to any one of claims 15 to 23, wherein the use is in treatment, prevention or recurrence suppression of intervertebral disc degeneration and/or intervertebral disc damage.

25. The composition for use according to claim 24, wherein the intervertebral disc degeneration and/or the intervertebral disc damage are at least one selected from the group consisting of intervertebral disc herniation, discopathy, degenerative spondylolisthesis, pyogenic discitis, chronic low back pain, spondylosis deformans, spinal canal stenosis, lumbar spinal stenosis, intervertebral disc herniation associated with lumbar spinal stenosis (combined lumbar spinal stenosis), and intervertebral disc damage.

26. The composition for use according to claim 24 or 25, wherein the intervertebral disc degeneration and/or the intervertebral disc damage are associated with chronic low back pain.

27. The composition for use according to any one of claims 15 to 23, wherein the use is to suppress intervertebral disc pain.

28. Use of the composition according to any one of claims 1 to 7 in the manufacture of a medicament for regeneration of the intervertebral disc, wherein regeneration of a nucleus pulposus of the intervertebral disc is promoted via activation of nucleus pulposus cells by the mesenchymal stem cells and/or differentiation of the mesenchymal stem cells into the nucleus pulposus cells.

29. The use according to claim 28, wherein the medicament is to be applied to the intervertebral disc of a subject and, after the application thereof, a crosslinking agent is to be brought into contact with at least a part of a surface of the medicament, and wherein the medicament has fluidity upon the application thereof.

30. The use according to claim 29, wherein the medicament is to be applied to a nucleus pulposus site of the intervertebral disc.

31. The use according to claim 30, wherein application of the medicament to the nucleus pulposus site comprises filling of the medicament into a defective site of the nucleus pulposus.

32. The use according to any one of claims 29 to 31, wherein the crosslinking agent is a divalent or higher valent metal ion compound.

33. The use according to any one of claims 28 to 32, wherein the medicament is for treatment, prevention or recurrence suppression of intervertebral disc degeneration and/or intervertebral disc damage.

34. The use according to claim 33, wherein the intervertebral disc degeneration and/or the intervertebral disc damage are at least one selected from the group consisting of intervertebral disc herniation, discopathy, degenerative spondylolisthesis, pyogenic discitis, spondylosis deformans, spinal canal stenosis, and intervertebral disc damage.

35. Use of a composition comprising a monovalent metal salt of alginic acid and human bone marrow-derived high-purity mesenchymal stem cells in the manufacture of a medicament for regeneration of an intervertebral disc, wherein the medicament is to be applied to a nucleus pulposus site of the intervertebral disc of a subject in a state in which the medicament has fluidity.

36. The use according to claim 35, wherein the medicament is to be then used without bringing a crosslinking agent into contact with the medicament.

37. The use according to claim 35 or 36, wherein regeneration of a nucleus pulposus of the intervertebral disc is promoted via activation of nucleus pulposus cells by the human bone marrow-derived high-purity mesenchymal stem cells and/or differentiation of the human bone marrow-derived high-purity mesenchymal stem cells into the nucleus pulposus cells.

38. The use according to any one of claims 35 to 37, wherein the human bone marrow-derived high-purity mesenchymal stem cells are in an undifferentiated state upon the application thereof and/or are to be applied without treatments of induction of differentiation.

39. The use according to any one of claims 35 to 38, wherein the human bone marrow-derived high-purity mesenchymal stem cells are a cell population of LNGFR (CD271)-positive, or LNGFR (CD271) and Thy-1 (CD90) double-positive, rapidly proliferating mesenchymal stem cell clones, said cell population satisfying at least one of the following characteristics (a) and (b):

(a) the coefficient of variation of forward scattered light in flow cytometry is 40% or less; and

(b) the average cell size is 20 μm or less.

40. The use according to any one of claims 35 to 39, wherein the human bone marrow-derived high-purity mesenchymal stem cells are a cell population of rapidly proliferating mesenchymal stem cell clones that are separated using, as an indicator, the feature that the cells are LNGFR (CD271)-positive, or LNGFR (CD271) and Thy-1 (CD90) double-positive cells, said cell population satisfying at least one of the following characteristics (a) and (b):

(a) the coefficient of variation of forward scattered light in flow cytometry is 40% or less; and

(b) the average cell size is 20 μm or less.

41. The use according to any one of claims 35 to 40, wherein the monovalent metal salt of alginic acid is a low endotoxin monovalent metal salt of alginic acid.

42. The use according to any one of claims 35 to 41, wherein the monovalent metal salt of alginic acid has a weight average molecular weight (absolute molecular weight) of 80,000 or more, as measured by a GPC-MALS method.

43. The use according to any one of claims 35 to 42, wherein the concentration of the monovalent metal salt of alginic acid is 0.5 w/w% to 5.0 w/w%.

44. The use according to any one of claims 35 to 43, wherein the medicament is for treatment, prevention or recurrence suppression of intervertebral disc degeneration and/or intervertebral disc damage.

45. The use according to claim 44, wherein the intervertebral disc degeneration and/or the intervertebral disc damage are at least one selected from the group consisting of intervertebral disc herniation, discopathy, degenerative spondylolisthesis, pyogenic discitis, chronic low back pain, spondylosis deformans, spinal canal stenosis, lumbar spinal stenosis, intervertebral disc herniation associated with lumbar spinal stenosis (combined lumbar spinal stenosis), and intervertebral disc damage.

46. The use according to claim 44 or 45, wherein the intervertebral disc degeneration and/or the intervertebral disc damage are associated with chronic low back pain.

47. The use according to any one of claims 35 to 43, wherein the medicament is to suppress intervertebral disc pain.