Claims

1. Use of a marker comprising an integrin alpha 10 subunit expressed by a neural stem cell and/or a neural progenitor cell as a marker for mammalian neural stem cells and mammalian neural progenitor cells.

2. A method for identifying a mammalian neural stem cell and/or a mammalian neural progenitor cell, the method comprising the steps of:
a) providing a sample comprising neural tissue,
b) detecting expression of an integrin alpha10 subunit by a cell comprised in the sample of a),
c) scoring the integrin alpha10 subunit expression of b), and
d) identifying the mammalian neural stem cell and/or the neural progenitor cell according to the scoring in c).

3. A method for isolating a mammalian neural stem cell and/or a mammalian neural progenitor cell, the method comprising the steps of:
a) providing a sample comprising neural tissue,
b) detecting expression of an integrin alpha10 subunit by a cell comprised in the sample of a),
c) scoring the integrin alpha10 subunit expression of b), and
d) selecting the mammalian neural stem cell and/or the mammalian neural progenitor cell according to the scoring in c).

4. The method or use according to any one of the preceding claims, wherein the integrin alpha 10 subunit is expressed on the cell surface of the mammalian neural stem cell and/or neural progenitor cell.

5. The method or use according to any one of the preceding claims, wherein the integrin alpha 10 subunit is expressed intracellularly in a mammalian neural stem cell and/or neural progenitor cell.

6. The method or use according to any one of the preceding claims, wherein the integrin alpha10 is expressed as a heterodimer in combination with an integrin beta1 subunit.

7. The method or the use according to any one of the preceding claims, further comprising a step of contacting the sample with an antibody which specifically binds integrin alpha10 subunit prior to the detection of b).

8. The method or the use according to any one of the preceding claims, further comprising detecting expression of a secondary marker selected from the group consisting of Nestin, PSA-NCAM, GFAP, PDFGRα, SOX-2, CD133 (prominin-1), CD15, CD24, Musashi, EGFR, Doublecortin (DCX), Pax6, FABP7, LeX, Vimentin and GLAST.

9. The method according to any one of the preceding claims, wherein the method is performed *in vitro*.

10. The method according to any one of the preceding claims, wherein the neural tissue comprises a neural stem cell and/or a neural progenitor cell.

11. The method according to any one of the preceding claims, wherein the neural tissue is obtained or derived from brain tissue.

12. The method according to any one of the preceding claims wherein the neural tissue is adult brain tissue.

13. The method according to any one of the preceding claims, wherein the neural tissue is fetal brain tissue.

14. The method according to any one of the preceding claims, wherein the neural tissue is derived from the subventricular zone (SVZ) or from the subgranular zone (SGZ) or from the meninges.

15. The method according to any one of the preceding claims, wherein the neural tissue is selected from the group consisting of human, canine, equine, bovine, feline, murine, ovine or swine neural tissue.

16. The method according to any one of the preceding claims, wherein the detection of expression of an integrin alpha10 subunit by a cell is determined by flow cytometry.

17. The method according to any one of the preceding claims, wherein the detection of expression of an integrin alpha10 subunit by a cell is determined by measuring integrin alpha10 protein expression.

18. The method according to any one of the preceding claims, wherein the detection of expression of an integrin alpha10 subunit by a cell is determined by measuring integrin alpha10 mRNA expression.

19. The method according to any one of the preceding claims, wherein the detection of expression of an integrin alpha10 subunit by a cell is determined by a method selected from the group consisting of immunoassay, immunoprecipitation, flow cytometry, immunofluorescence, and western blot.

20. The method according to any one of the preceding claims, wherein the antibody used for detection of expression of an integrin alpha10 subunit by a cell is a monoclonal antibody, polyclonal antibody, a chimeric antibody, a single chain antibody or fragment thereof.

21. The method according to any one of the preceding claims, wherein the antibody is a monoclonal antibody.

22. The method according to any one of the preceding claims, wherein the antibody is a non-human antibody, a chimeric antibody, a bispecific antibody, a humanized antibody or a human antibody.

23. The method according to any one of the preceding claims, wherein the antibody is covalently bound to a detectable moiety, such as a detectable moiety selected from the group consisting of a fluorophore, an enzyme or a radioactive tracer or radioisotope.

24. The method according to any one of the preceding claims, wherein the antibody has an isotype selected from the group consisting of IgA, IgD, IgG and IgM.

25. The method according to any one of the preceding claims, wherein the antibody is: a) a monoclonal antibody, produced by the hybridoma cell line deposited at the Deutsche Sammlung von Microorganismen und Zellkulturen GmbH under

the accession number DSM ACC2583; or

b) an antibody which competes for binding to the same epitope as the epitope bound by the monoclonal antibody produced by the hybridoma deposited at the Deutsche Sammlung von Microorganismen und Zellkulturen GmbH under the accession number DSM ACC2583; or

c) a fragment of a) or b), wherein said fragment is capable of binding specifically to the extracellular I-domain of the integrin alpha 10 subunit chain.

26. The method of any one of the preceding claims, wherein the antibody is attached to a solid support.

27. The method according to any one of the preceding claims, wherein the antibody is labeled with one or more fluorophore(s).

28. The method according to any one of the preceding claims, wherein the fluorophore is phycoerythrin, allophycocyanin, fluorescein, Texas red, or Alexa Fluor 647, brilliant dyes.

29. The method according to any one of the preceding claims wherein the antibody further comprises a moiety suitable for detection.

30. The method according to any one of the preceding claims, wherein the moiety suitable for detection is selected from nanoparticles, and radioisotopes.

31. The method according to any one of the preceding claims, wherein the nanoparticle is selected from the group consisting of micelles, inelastic shells, nanotubular particles, liposomes, gold nanoparticles and polymers.

32. The method according to any one of the preceding claims, wherein the radioisotope is selected from the group consisting of beta-emitters, auger-emitters, conversion electron-emitters, alpha-emitters, and low photon energy-emitters.

33. The method according to any one of the preceding claims, wherein the detectable moiety comprises or consists of a paramagnetic isotope.

34. The method according to any one of the preceding claims, wherein the paramagnetic isotope is selected from the group consisting of ^{157}Gd, ^{55}Mn, ^{162}Dy, ^{52}Cr and ^{56}Fe.

35. The method according to any one of the preceding claims, wherein the detectable moiety is detectable by an imaging technique such as SPECT, PET, MRI, optical or ultrasound imaging.

36. A method for determining whether a test compound modulates a mammalian neural stem cell and/or a mammalian neural progenitor cell differentiation *in vitro*, the method comprising the steps of

a) providing a neural stem cell and/or a neural progenitor cell that expresses, or has the ability to express, an integrin alpha10 subunit,

b) contacting the neural stem cell and/or the neural progenitor cell with a test compound, and

c) detecting a change in rate or pattern of differentiation of the neural stem cell and/or neural progenitor cell as an indication of that the test compound modulates a neural stem cell and/or a neural progenitor cell differentiation,

wherein the rate or pattern of differentiation is determined by detecting integrin alpha10 expression by the cell according to the method in any one of claims 2 to 35.

37. A method for manufacturing an isolated population of mammalian cells *in vitro* which are enriched for neural stem cells and/or neural progenitor cells relative to a reference population, the method comprising the steps of

a) providing at least a portion of a population of cells, or a portion of a reference population, comprising a neural stem cell and/or a neural progenitor cell,

b) introducing into the population of cells in a) above a compound identifying an integrin alpha10 subunit expressed by the neural stem cell and/or neural progenitor cell,

c) selecting and isolating, or isolating and selecting, or isolating, or selecting, the neural stem cells and/or the neural progenitor cells from the population of cells in step b) above,

thereby producing a population of cells enriched for neural stem cells and/or neural progenitor cells.

38. The method according to claim 37, wherein the neural stem cells and/or the neural progenitor cells are identified and/or isolated by the method as defined in in any one of claims 2 to 35.

39. The method according to any one of claims 37 and 38, wherein the selection in step c) is performed by fluorescent cell sorting or magnetic bead sorting.

40. An *in vitro* cell culture of undifferentiated mammalian cells expressing an integrin alpha10 subunit, wherein the cells are derived from neural tissue and wherein
    a) cells in the culture have the capacity to differentiate into neurons and/or oligodendrocytes and/or astrocytes when differentiated in a culture medium substantially free of both serum and a proliferation-inducing growth factor as defined in (b) to produce a cell culture of at least 10% neurons and/or oligodendrocytes and/or astrocytes;
    b) the cell culture divides in a culture medium containing a serum replacement such as B27 and at least one proliferation-inducing growth factor;
    c) cells in the culture differentiate into neurons and/or oligodendrocytes and/or astrocytes upon withdrawal of both the serum replacement and the proliferation inducing growth factor.

41. An *in vitro* cell culture comprising
    a) a culture medium containing a serum replacement such as B27 and at least one proliferation-inducing growth factor; and
    b) undifferentiated mammalian cells derived from the central nervous system of a mammal, wherein at wherein at least 10%, preferably at least 20%, preferably at least 30%, preferably at least 40%, preferably at least 50%, preferably at least 60%, preferably at least 70%, preferably at least 80%, preferably at least 90% of the cells express an integrin alpha10 subunit.

42. A suspension culture of mammalian undifferentiated cells expressing an integrin alpha10 subunit, wherein said cells are substantially formed into cell aggregates, and wherein the cell aggregates are maintained in a culture medium containing a proliferation-inducing growth factor.

43. A cell culture obtainable by the method according to any one of claims 3 to 28.

44. The cell culture or the suspension culture according to any one of claims 40 to 42, wherein the integrin alpha10 is expressed as a heterodimer in combination with an integrin beta1 chain.

45. The cell culture or the suspension culture according to any one of claims 40 to 44, wherein the integrin alpha 10 subunit is expressed on the cell surface of the undifferentiated mammalian cell.

46. The cell culture or the suspension culture according to any one of claims 40 to 45, wherein the integrin alpha 10 subunit is expressed intracellularly in the undifferentiated mammalian cell.

47. The cell culture or the suspension culture according to any one of claims 40 to 46, wherein at least 10%, preferably at least 20%, preferably at least 30%, preferably at least 40%, preferably at least 50%, preferably at least 60%, preferably at least 70%, preferably at least 80%, preferably at least 90% of the undifferentiated mammalian cells are mammalian neural stem cells expressing a integrin alpha10 subunit.

48. The cell culture or the suspension culture according to any one of claims 40 to 47, wherein the undifferentiated mammalian cell is a neural stem cell or a neural progenitor cell.

49. The cell culture or the suspension culture according to any one of claims 40 to 48, wherein a part of the cells in the culture further expresses at least one marker selected from the group consisting of nestin, PSA-NCAM, GFAP, SOX2, PDGFRα, CD133, CD15, CD24, Musashi, EGFR, Doublecortin (DCX), Pax6, FABP7 and GLAST.

50. The cell culture or the suspension culture according to any one of claims 40 to 49, wherein the at least one proliferation-inducing growth factor is selected from a group consisting of epidermal growth factor (EGF), fibroblast growth factor-2 (FGF-2), Transforming growth factor alpha (TGF-α), Leukemia inhibitory factor (LIF), Ciliary neurotropic factor (CNTF), Brain-derived neurotrophic factor (BDNF), PDGFα or combinations thereof.

51. The cell culture or the suspension culture according to any one of claims 40 to 50, wherein the cells in the culture are obtained or derived from the subventricual zone (SVZ) or from the subgranular zone (SGZ) or from the meninges of a mammalian brain.

52. The cell culture or the suspension culture according to any one of claims 40 to 51, wherein the cells in the culture are murine.

53. The cell culture or the suspension culture according to any one of claims 40 to 52, wherein the cells in the culture are human.

54. The cell culture or the suspension culture according to any one of claims 40 to 53, wherein the cells in the culture are derived from human fetal or human adult neural stem cells and/or neural progenitor cells.

55. The cell culture or the suspension culture according to any one of claims 40 to 54, wherein the cells in the culture are not derived from human embryonic cells or from a human embryo.

56. A method of treating disease or damage and/or preventing and protecting from damage of the nervous system in a subject in need thereof, the method comprising:
    a) providing a composition comprising an enriched population of mammalian neural stem cells and/or mammalian neural progenitor cells, wherein the cells express an integrin alpha10 subunit;
    b) administering a therapeutically effective amount of the isolated population of mammalian neural stem cells and/or neural progenitor cells to the subject,

thereby treating the disease or damage and/or preventing and protecting from damage of the central nervous system.

57. A method of treating a mental and behavioral disorder in a subject in need thereof, the method comprising:
    a) providing a composition comprising an enriched population of mammalian neural stem cells and/or mammalian neural progenitor cells, wherein the cells express an integrin alpha10 subunit;
    b) administering a therapeutically effective amount of the isolated population of mammalian neural stem cells and/or neural progenitor cells to the subject,

    thereby treating the neurologic disorders with psychiatric symptoms.

58. A method of treating disease or damage and/or preventing and protecting from damage of the nervous system in a subject in need thereof, the method comprising:
    a) providing a composition comprising an enriched population of mammalian mesenchymal stem cells, wherein the cells express integrin alpha10 subunit;
    b) administering a therapeutically effective amount of the isolated population of mammalian mesenchymal stem cells to the subject,

    thereby treating the disease or damage and/or preventing and protecting from damage of the central nervous system.

59. A method of treating a mental or behavioral disorder in a subject in need thereof, the method comprising:
    a) providing a composition comprising an enriched population of mammalian mesenchymal stem cells, wherein the cells express integrin alpha10 subunit;
    b) administering a therapeutically effective amount of the isolated population of mammalian mesenchymal stem cells to the subject,

    thereby treating the neurologic disorders with psychiatric symptoms.

60. The method according to any one of claims 58 and 59 wherein the mammalian mesenchymal stem cells are isolated from bone marrow or adipose tissue or cord blood or Wharton's jelly or dental pulp or cord tissue or blood or amniotic fluid or amniotic membrane or endometrium or limb bud or salivary gland or skin or foreskin or synovial membrane .

61. An in vitro method for determining the characteristics of a damaged or diseased area of the CNS in a patient in need thereof, the method comprising the steps of:
    a) administering an anti-integrin alpha 10 subunit to a subject,
    b) detecting expression of integrin alpha10 subunit in the damaged or diseased area of the CNS of the subject,
    c) determining characteristics such as location and size of the damaged or diseased area of the CNS.

62. The method according to claim 61 wherein, the neural tissue comprises neural stem cells and/or neural progenitor cells.

63. The method according to claim 61, wherein the characteristics is used to predict the degree of regeneration of CNS tissue after stroke.

64. The method according to any one of claims 61 to 63, wherein a high value of expression of integrin alpha10 subunit corresponds to a low value of the modified Rankin Scale (mRS).

65. The method according to any one of claims 61 to 64, wherein the integrin alpha10 subunit is used in a biomarker panel.

66. A marker for mammalian neural stem cells and/or mammalian neural progenitor cells, comprising an integrin alpha10 chain subunit expressed by the neural stem cell and/or neural progenitor cells, for use in a method of treating a disease or damage and/or for preventing and protecting from damage of the nervous system and/or for treating a mental and behavioral disorder, or for diagnosing and/or characterizing the disease or damage.

67. A composition comprising an isolated population of mammalian neural stem cells and/or mammalian neural progenitor cells expressing an integrin alpha10 subunit for use in a method of treatment of disease or damage of the nervous system and/or mental and behavioral disorder

68. The method, the marker or the composition according to any one of claims 56 to 67, wherein the integrin alpha10 is expressed as a heterodimer in combination with an integrin beta1 chain.

69. The method, the marker or the composition according to any one of claims 56 to 68, wherein the integrin alpha10 subunit is expressed on the cell surface of the mammalian neural stem cell and/or neural progenitor cell.

70. The method, the marker or the composition according to any one of claims 56 to 69, wherein the integrin alpha 10 subunit is expressed intracellularly in a mammalian neural stem cell and/or neural progenitor cell.

71. The method, the marker or the composition according to any one of claims 56 to 70, wherein the population of cells is enriched for mammalian neural stem cells and/or mammalian neural progenitor cells expressing an integrin alpha10 subunit.

72. The method, the marker or the composition according to any one of claims 56 to 71, wherein disease or damage of the nervous system is an injury of the central or peripheral nervous system or a neurodegenerative disease.

73. The method, the marker or the composition according to any one of claims 56 to 72, wherein the injury of the nervous system is selected from a group consisting of spinal cord injuries (SCI), traumatic brain injuries (TBI), peripheral nerve injuries, stroke and brain cancer.

74. The method, the marker or composition according to any one of claims 56 to 73, wherein the injury of the nervous system is stroke.

75. The method, the marker or the composition according to any one of claims 56 to 73, wherein the neurodegenerative diseases are selected from a group consisting of Alzheimer's disease, Parkinson's disease, amyotrophic lateral

sclerosis (ALS), Huntington's Disease (HD), multiple sclerosis (MS) and multiple system atrophy.

76. The method, the marker for use, or the composition according to any one of claims 56 to 73, wherein the mental or behavioral disorder is selected from the group consisting of Rett syndrome, schizophrenia, depression, autism spectrum disorders (ASD) and bipolar disorder (BPD).

77. The method, the marker for use, or the composition according to any one of claims 56 to 73, wherein said neural stem cells are isolated using the method as defined in any one of claims 2 to 55, or wherein said neural stem cells are as defined in any one of claims 2 to 55.

78. The method, the marker for use, or the composition according to any one of the preceding claims wherein the neural stem cell is an allogenic neural stem cell.

79. The method, the marker for use, or the composition according to any one of the preceding claims wherein the neural stem cell is an autologous neural stem cell.

80. The method, the marker for use, or the composition according to any one of the preceding claims wherein the neural progenitor cell is an allogenic neural progenitor cell.

81. The method, the marker for use, or the composition according to any one of the preceding claims wherein the neural progenitor cell is an autologous neural progenitor cell.

82. The method, the marker for use, or the composition according to any one of the preceding claims wherein the mesenchymal stem cell is an allogenic mesenchymal stem cell.

83. The method, the marker for use, or the composition according to any one of the preceding claims wherein the mesenchymal stem cell is an autologous mesenchymal stem cell.