

CLAIMS

1. A human-derived recombinant monoclonal anti-Nogo-A antibody or antigen-binding fragment thereof, wherein the antibody or antigen-binding fragment thereof binds to the Nogo-A- Δ 20 domain and is capable of inducing dose dependent neurite outgrowth and/or angiogenesis in stroke penumbra.
2. The antibody or antigen-binding fragment thereof of claim 1, wherein the antibody or antigen-binding fragment thereof binds to a peptide comprising or consisting of the amino acid sequence of SEQ ID NO: 21 and/or comprises a variable heavy (VH) chain comprising VH complementary determining regions (CDRs) 1, 2, and 3, and a variable light (VL) chain comprising VL CDRs 1, 2, and 3, wherein
- (a) VH-CDR1 comprises the amino acid sequence of SEQ ID NO: 3 or a variant thereof, wherein the variant comprises one or two amino acid substitutions,
 - (b) VH-CDR2 comprises the amino acid sequence of SEQ ID NO: 4 or a variant thereof, wherein the variant comprises one or two amino acid substitutions,
 - (c) VH-CDR3 comprises the amino acid sequence of SEQ ID NO: 5 or a variant thereof, wherein the variant comprises one or two amino acid substitutions,
 - (d) VL-CDR1 comprises the amino acid sequence of SEQ ID NO: 8 or a variant thereof, wherein the variant comprises one or two amino acid substitutions,
 - (e) VL-CDR2 comprises the amino acid sequence of SEQ ID NO: 9 or a variant thereof, wherein the variant comprises one or two amino acid substitutions, and
 - (f) VL-CDR3 comprises the amino acid sequence of SEQ ID NO: 10 or a variant thereof, wherein the variant comprises one or two amino acid substitutions; or wherein the antibody comprises a VH chain comprising CDRs 1, 2, and 3, and/or a VL chain comprising VL CDRs 1, 2, and 3, wherein
 - (g) VH-CDR1 comprises the amino acid sequence of SEQ ID NO: 13 or a variant thereof, wherein the variant comprises one or two amino acid substitutions,
 - (h) VH-CDR2 comprises the amino acid sequence of SEQ ID NO: 14 or a variant thereof, wherein the variant comprises one or two amino acid substitutions,
 - (i) VH-CDR3 comprises the amino acid sequence of SEQ ID NO: 15 or a variant thereof, wherein the variant comprises one or two amino acid substitutions,
 - (j) VL-CDR1 comprises the amino acid sequence of SEQ ID NO: 18 or a variant thereof, wherein the variant comprises one or two amino acid substitutions,

- (k) VL-CDR2 comprises the amino acid sequence of SEQ ID NO: 19 or a variant thereof, wherein the variant comprises one or two amino acid substitutions, and
- (l) VL-CDR3 comprises the amino acid sequence of SEQ ID NO: 20 or a variant thereof, wherein the variant comprises one or two amino acid substitutions.
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3. The antibody or antigen-binding fragment thereof of claim 1 or 2, wherein:
- (a) the VH comprises the amino acid sequence depicted in SEQ ID NO: 2 or a variant thereof, wherein the variant comprises one or more amino acid substitutions; and
- 10 (b) the VL comprises the amino acid sequence depicted in SEQ ID NO: 7, or a variant thereof, wherein the variant comprises one or more amino acid substitutions; preferably wherein the VH and VL amino acid sequence is at least 90% identical to SEQ ID NO: 2 and 7, respectively; or
- 15 (c) the VH chain comprises the amino acid sequence depicted in SEQ ID NO: 12 or a variant thereof, wherein the variant comprises one or more amino acid substitutions; and
- (d) the VL comprises the amino acid sequence depicted in SEQ ID NO: 17, or a variant thereof, wherein the variant comprises one or more amino acid
- 20 substitutions; preferably wherein the VH and VL chain amino acid sequence is at least 90% identical to SEQ ID NO: 12 and 17, respectively.
4. The antibody or antigen-binding fragment thereof of any one of claims 1 to 3 further comprising an immunoglobulin heavy chain constant region, an immunoglobulin light chain constant region, preferably wherein the immunoglobulin heavy and/or light chain constant region is of the IgG type.
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5. The antibody or antigen-binding fragment thereof of any one of claims 1 to 4, comprising a constant domain Fc region with reduced effector functions compared to IgG; preferably wherein the constant domain of the IgG4 class.
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6. The antibody or antigen-binding fragment thereof of claim 5, which is of the IgG4 class or isotype including the S228P mutation.

7. The antibody or antigen-binding fragment thereof of any one of claims 1 to 6, which is selected from the group consisting of a single chain Fv fragment (scFv), an F(ab') fragment, an F(ab) fragment, and an F(ab')₂ fragment, an Fd, an Fv, a single-chain antibody, and a disulfide-linked Fv (sdFv) and/or which is a chimeric murine-human antibody.
8. One or more polynucleotide(s) encoding the antibody or antigen-binding fragment thereof of any one of claims 1 to 7 or an immunoglobulin VH and VL thereof, preferably wherein the polynucleotide is a cDNA and/or operably linked to a heterologous nucleic acid.
9. One or more vector(s) comprising the polynucleotide(s) of claim 8.
10. A host cell comprising the polynucleotide(s) of claim 8 or the vector(s) of claim 9.
11. A method for preparing an anti-Nogo-A antibody, antigen-binding fragment or immunoglobulin chain(s) thereof, said method comprising
- (a) culturing the cell of claim 10; and
 - (b) isolating the antibody, antigen-binding fragment or immunoglobulin chain(s) thereof from the culture.
12. An antibody, antigen-binding fragment or immunoglobulin chain(s) thereof encoded by the polynucleotide(s) of claim 8 or obtainable by the method of claim 11.
13. An antibody or antigen-binding fragment thereof of any one of claims 1 to 7 or the antibody or antigen-binding fragment thereof of claim 12, which is
- (i) detectably labeled with a label selected from the group consisting of an enzyme, a radioisotope, a fluorescent compound, a chemiluminescent compound, a bioluminescent compound, a tag, a flag and a heavy metal;
 - (ii) attached to a drug; or
 - (iii) comprises polyethylene glycol.

14. A composition comprising the antibody or antigen-binding fragment thereof of any one of claims 1 to 7, 12 or 13, the polynucleotide(s) of claim 8, the vector(s) of claim 9 or the cell of claim 10, preferably the composition is
- 5 (i) a pharmaceutical composition and further comprises a pharmaceutically acceptable carrier; or
- (ii) a diagnostic composition and designed as a kit, optionally further comprising reagents conventionally used in immuno-based diagnostic methods.
15. An antibody or antigen-binding fragment thereof of any one of claims 1 to 7, 12 or 13, 10 the polynucleotide(s) of claim 8, the vector(s) of claim 9 or the cell of claim 10 for use in the treatment of a disease or trauma of the peripheral (PNS) and/or central (CNS) nervous system including the retina or for use in *in vivo* detection of Nogo-A in the human or animal body, preferably wherein the disease is a neurodegenerative disease selected from the group consisting of Alzheimer disease, Parkinson disease, 15 Amyotrophic lateral sclerosis (ALS), Lewy like pathologies and other dementia in general, diseases following cranial, cerebral or spinal trauma, stroke, traumatic brain injury, a demyelinating disease and a ophthalmologic disease selected from the group consisting of diabetic retinopathy, diabetic macular edema, wet and dry age-related macular degeneration (AMD), and other ophthalmological indications.

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