WHAT IS CLAIMED IS:

1. A human monoclonal anti-TAR-DNA-binding protein 43kDa (TDP-43) antibody.

2. A monoclonal anti-TDP-43 antibody which specifically binds a TDP-43 polypeptide consisting of an amino acid sequence selected from the group consisting of:

(a) amino acid residues 2-106 of SEQ ID NO:94;

(b) amino acid residues 99-204 of SEQ ID NO:94;

(c) amino acid residues 183-273 of SEQ ID NO:94;

(d) amino acid residues 258-414 of SEQ ID NO:94; and

(e) amino acid residues 390-414 of SEQ ID NO:94, wherein the serine at least one of positions 409 and 410 is phosphorylated.

3. The monoclonal antibody of claim 2 wherein the antibody specifically binds a TDP-43 polypeptide consisting of amino acid residues 258-414 of SEQ ID NO:94, but does not bind the TDP-43 258-414 AMM321GGG polypeptide.

4. A monoclonal anti-TDP-43 antibody which specifically binds a TDP-43 polypeptide comprising an amino acid sequence selected from the group consisting of QYGDVMDVFIP (SEQ ID NO: 123); AAIGWGSASNA (SEQ ID NO: 124); DMTEDELREFF (SEQ ID NO: 125), EDENDEP (SEQ ID NO: 126), VQVKKDL (SEQ ID NO: 127), KEYFSTF (SEQ ID NO: 128), IIKGISV (SEQ ID NO:315), NQSGPSG (SEQ ID NO:316), FNGGFGS (SEQ ID NO:317), FGNSRGGGAGL (SEQ ID NO:318), SNAGSGSGFNG (SEQ ID NO:319), QLERSGRFGGN (SEQ ID NO:320), EIPSEDD (SEQ ID NO:321), FNGGFGSSMDS (SEQ ID NO:322), SINPAMMAAAQAALQSSWGMMGMLASQ (SEQ ID NO:323), and any combinations thereof.

5. The monoclonal antibody of claim 4 wherein the antibody specifically binds a TDP-43 polypeptide comprising the amino acid sequence of FGNSRGGGAGL (SEQ ID NO:318)

and a TDP-43 polypeptide comprising the amino acid sequence of SNAGSGSGFNG (SEQ ID NO:319).

6. The monoclonal antibody of claim 4 wherein the antibody specifically binds a TDP-43 polypeptide comprising the amino acid sequence of SINPAMMAAAQAALQSSWGMMGMLASQ (SEQ ID NO:323), but does not bind to a polypeptide comprising the amino acid sequence of SINPGGGAAAQAALQSSWGMMGMLASQ (SEQ ID NO:314).

7. The monoclonal anti-TDP-43 antibody of any one of claims 1-6 which specifically binds to a pathologic form of human TDP-43.

8. The monoclonal anti-TDP-43 antibody of any one of claims 1-6 which specifically binds to any combination of full length, truncated, or pathologic human TDP-43 in an immunohistochemistry.

9. A monoclonal anti-TDP-43 antibody of any one of claims 1-6 which specifically binds to cytoplasmic or neuritic TDP-43 in human brain tissue.

10. The monoclonal anti-TDP-43 antibody of any one of claims 1-9 comprising a heavy chain variable region VH, wherein the heavy chain variable region comprises one, two or three VH CDRs of an antibody selected from the group consisting of: NI-205.3F10, NI-205.51C1, NI-205.21G2, NI-205.8A2, NI-205.15F12, NI-205.113C4, NI-205.25F3, NI-205.87E7, NI-205.21G1, NI-205.68G5, NI-205.20A1, NI205.41D1, NI205.29E11, NI205.9E12, NI205.98H6, NI205.10D3, NI205.44B2, NI205.38H2, NI205.36D5, NI205.58E11, NI205.14H5, NI205.31D2, NI205.8F8, NI205.31C11, NI205.8C10, NI205.10H7, NI205.1A9, NI205.14W3, and NI205.19G5.

11. The monoclonal anti-TDP-43 antibody of claim 10 comprising a VH CDR1, VH CDR2, and VH CDR3 of an antibody selected from the group consisting of: NI-205.3F10, NI-205.51C1, NI-205.21G2, NI-205.8A2, NI-205.15F12, NI-205.113C4, NI-205.25F3, NI-205.87E7, NI-205.21G1, NI-205.68G5, NI-205.20A1, NI205.41D1, NI205.29E11, NI205.9E12, NI205.98H6, NI205.10D3, NI205.44B2, NI205.38H2, NI205.36D5, NI205.58E11, NI205.14H5, NI205.31D2, NI205.8F8, NI205.31C11, NI205.8C10, NI205.10H7, NI205.1A9, NI205.14W3, and NI205.19G5.

12. The monoclonal anti-TDP-43 antibody of claim 10 comprising one or more of:

(a) a VH CDR1 selected from the group consisting of: SEQ ID NO: 11, 19, 28, 37, 46, 54, 62, 70, 79, 88, 131, 139, 147, 156, 164, 172, 180, 188, 196, 204, 212, 220, 228, 236, 244, 252, 260, and 268 ;

(b) a VH CDR2 selected from the group consisting of: SEQ ID NO: 4, 12, 20, 29, 38, 47, 55, 63, 71, 80, 89, 132, 140, 148, 157, 165, 173, 181, 189, 197, 205, 213, 221, 229, 237, 245, 253, 261, and 269; and

(c) a VH CDR3 selected from the group consisting of: SEQ ID NO: 5, 13, 21, 30, 39, 48, 56, 64, 72, 81, 90, 133, 141, 149, 158, 166, 174, 182, 190, 198, 206, 214, 222, 230, 238, 246, 254, 262, and 270.

13. The monoclonal anti-TDP-43 antibody of claim 11 comprising:

(a) a VH CDR1 selected from the group consisting of: SEQ ID NO: 11, 19, 28, 37, 46, 54, 62, 70, 79, 88, 131, 139, 147, 156, 164, 172, 180, 188, 196, 204, 212, 220, 228, 236, 244, 252, 260, and 268 ;

(b) a VH CDR2 selected from the group consisting of: SEQ ID NO: 4, 12, 20, 29, 38, 47, 55, 63, 71, 80, 89, 132, 140, 148, 157, 165, 173, 181, 189, 197, 205, 213, 221, 229, 237, 245, 253, 261, and 269; and

(c) a VH CDR3 selected from the group consisting of: SEQ ID NO: 5, 13, 21, 30, 39, 48, 56, 64, 72, 81, 90, 133, 141, 149, 158, 166, 174, 182, 190, 198, 206, 214, 222, 230, 238, 246, 254, 262, and 270.

14. The monoclonal anti-TDP-43 antibody of claim 13 comprising the VH CDR1, VH CDR2, and VH CDR3 of an antibody selected from the group consisting of: NI-205.3F10, NI-205.51C1, NI-205.21G2, NI-205.8A2, NI-205.15F12, NI-205.113C4, NI-205.25F3, NI-205.87E7, NI-205.21G1, NI-205.68G5, NI-205.20A1, NI205.41D1, NI205.29E11, NI205.9E12, NI205.98H6, NI205.10D3, NI205.44B2, NI205.38H2, NI205.36D5, NI205.58E11, NI205.14H5, NI205.31D2, NI205.8F8, NI205.31C11, NI205.8C10, NI205.10H7, NI205.1A9, NI205.14W3, and NI205.19G5, wherein the VH CDR1, VH CDR2, and VH CDR3 are defined as listed in Table 2.

15. The monoclonal anti-TDP-43 antibody of any one of claims 1-14 comprising a light chain variable region VL, wherein the light chain variable region comprises one, two or three VL CDRs of an antibody selected from the group consisting of: NI-205.3F10, NI-205.51C1, NI-205.21G2, NI-205.8A2, NI-205.15F12, NI-205.113C4, NI-205.25F3, NI-205.87E7, NI-205.21G1, NI-205.68G5, NI-205.20A1, NI205.41D1, NI205.29E11, NI205.9E12, NI205.98H6, NI205.10D3, NI205.44B2, NI205.38H2, NI205.36D5, NI205.58E11, NI205.14H5, NI205.31D2, NI205.8F8, NI205.31C11, NI205.8C10, NI205.10H7, NI205.1A9, NI205.14W3, and NI205.19G5.

16. The monoclonal anti-TDP-43 antibody of claim 15 comprising a VL CDR1, VL CDR2, and VL CDR3 of an antibody selected from the group consisting of: NI-205.3F10, NI-205.51C1, NI-205.21G2, NI-205.8A2, NI-205.15F12, NI-205.113C4, NI-205.25F3, NI-205.87E7, NI-205.21G1, NI-205.68G5, NI-205.20A1, NI205.41D1, NI205.29E11, NI205.9E12, NI205.98H6, NI205.10D3, NI205.44B2, NI205.38H2, NI205.36D5, NI205.58E11, NI205.14H5, NI205.31D2, NI205.8F8, NI205.31C11, NI205.8C10, NI205.10H7, NI205.1A9, NI205.14W3, and NI205.19G5.

17. The monoclonal anti-TDP-43 antibody of claim 15 comprising one or more of:

(a) a VL CDR1 selected from the group consisting of: SEQ ID NO: 7, 15, 23, 32, 42, 50, 58, 66, 74, 84, 91, 135, 143, 152, 160, 168, 176, 184, 192, 200, 208, 216, 224, 232, 240, 248, 256, 264, 272 and 326;

(b) a VL CDR2 selected from the group consisting of: SEQ ID NO: 8, 16, 24, 33, 43, 51, 59, 67, 75, 85, 92, 136, 144, 153, 161, 169, 177, 185, 193, 201, 209, 217, 225, 233, 241, 249, 257, 265, 273 and 327; and

(c) a VL CDR3 selected from the group consisting of: SEQ ID NO: 9, 17, 25, 34, 44, 52, 60, 68, 76, 86, 93, 137, 145, 154, 162, 170, 178, 186, 194, 202, 210, 218, 226, 234, 242, 250, 258, 266, 274 and 328.

18. The monoclonal anti-TDP-43 antibody of claim 17 comprising:

(a) a VL CDR1 selected from the group consisting of: SEQ ID NO: 7, 15, 23, 32, 42, 50, 58, 66, 74, 84, 91, 135, 143, 152, 160, 168, 176, 184, 192, 200, 208, 216, 224, 232, 240, 248, 256, 264, 272 and 326;

(b) a VL CDR2 selected from the group consisting of: SEQ ID NO: 8, 16, 24, 33, 43, 51, 59, 67, 75, 85, 92, 136, 144, 153, 161, 169, 177, 185, 193, 201, 209, 217, 225, 233, 241, 249, 257, 265, 273 and 327; and

(c) a VL CDR3 selected from the group consisting of: SEQ ID NO: 9, 17, 25, 34, 44, 52, 60, 68, 76, 86, 93, 137, 145, 154, 162, 170, 178, 186, 194, 202, 210, 218, 226, 234, 242, 250, 258, 266, 274 and 328.

19. The monoclonal anti-TDP-43 antibody of claim 18 comprising the VL CDR1, VL CDR2, and VL CDR3 of an antibody selected from the group consisting of: NI-205.3F10, NI-205.51C1, NI-205.21G2, NI-205.8A2, NI-205.15F12, NI-205.113C4, NI-205.25F3, NI-205.87E7, NI-205.21G1, NI-205.68G5, NI-205.20A1, NI205.41D1, NI205.29E11, NI205.9E12, NI205.98H6, NI205.10D3, NI205.44B2, NI205.38H2, NI205.36D5, NI205.58E11, NI205.14H5, NI205.31D2, NI205.8F8, NI205.31C11, NI205.8C10, NI205.10H7, NI205.1A9, NI205.14W3, and NI205.19G5, wherein the VL CDR1, VL CDR2, and VL CDR3 are defined as listed in Table 2

20. The monoclonal anti-TDP-43 antibody of any one of claims 1-19 comprising a heavy chain variable region VH at least 80%, 85%, 90%, 95%, 96%, 97%, 98% or 99% identical to an amino acid sequence selected from the group consisting of: SEQ ID NO: 1, 10, 18, 26, 35, 45, 53, 61, 69, 77, 87, 130, 138, 146, 155, 163, 171, 179, 187, 195, 203, 211, 219, 227, 235, 243, 251, 259, and 267.

21. The monoclonal anti-TDP-43 antibody of claim 20, wherein the heavy chain variable region comprises an amino acid sequence selected from the group consisting of: SEQ ID NO: 1, 10, 18, 26, 35, 45, 53, 61, 69, 77, 87, 130, 138, 146, 155, 163, 171, 179, 187, 195, 203, 211, 219, 227, 235, 243, 251, 259, and 267.

22. The monoclonal anti-TDP-43 antibody of any one of claims 1-21 comprising a light chain variable region VL at least 80%, 85%, 90%, 95%, 96%, 97%, 98% or 99% identical to an amino acid sequence selected from the group consisting of: SEQ ID NO: 6, 14, 22, 31,

40, 49, 57, 65 ,73, 82, 122, 134, 142, 150, 151, 159, 167, 175, 183, 191, 199, 207, 215, 223, 231, 239, 247, 255, 263, and 271.

23. The monoclonal anti-TDP-43 antibody of claim 22, wherein the light chain variable region comprises an amino acid sequence selected from the group consisting of: SEQ ID NO: 6, 14, 22, 31, 40, 49, 57, 65 ,73, 82, 122, 134, 142, 150, 151, 159, 167, 175, 183, 191, 199, 207, 215, 223, 231, 239, 247, 255, 263, and 271.

24. The monoclonal anti-TDP-43 antibody of any one of claims 1-16 comprising a VH and VL pair selected from the group consisting of: a VH of SEQ ID NO: 1 and a VL of SEQ ID NO: 6, a VH of SEQ ID NO: 10 and a VL of SEQ ID NO: 14, a VH of SEQ ID NO: 18 and a VL of SEQ ID NO: 22, a VH of SEQ ID NO: 26 and a VL of SEQ ID NO: 31, a VH of SEQ ID NO: 35 and a VL of SEQ ID NO: 40, a VH of SEQ ID NO:45 and a VL of SEQ ID NO: 49, a VH of SEQ ID NO: 53 and a VL of SEQ ID NO: 57, a VH of SEQ ID NO: 61 and a VL of SEQ ID NO: 65, a VH of SEQ ID NO: 69 and a VL of SEQ ID NO: 73, a VH of SEQ ID NO: 77 and a VL of SEQ ID NO: 82, a VH of SEQ ID NO:87 and a VL of SEQ ID NO: 122, a VH of SEQ ID NO:130 and a VL of SEQ ID NO: 134, a VH of SEQ ID NO:138 and a VL of SEQ ID NO: 142, a VH of SEQ ID NO:146 and a VL of SEQ ID NO: 150, a VH of SEQ ID NO:146 and a VL of SEQ ID NO: 151, a VH of SEQ ID NO:155 and a VL of SEQ ID NO: 159, a VH of SEQ ID NO:163 and a VL of SEQ ID NO: 167, a VH of SEQ ID NO:171 and a VL of SEQ ID NO: 175, a VH of SEQ ID NO:179 and a VL of SEQ ID NO: 183, a VH of SEQ ID NO:187 and a VL of SEQ ID NO: 191, a VH of SEQ ID NO:195 and a VL of SEQ ID NO: 199, a VH of SEQ ID NO:203 and a VL of SEQ ID NO: 207, a VH of SEQ ID NO:211 and a VL of SEQ ID NO: 215, a VH of SEQ ID NO:219 and a VL of SEQ ID NO: 223, a VH of SEQ ID NO:227 and a VL of SEQ ID NO: 231, a VH of SEQ ID NO:235 and a VL of SEQ ID NO: 239, a VH of SEQ ID NO:243 and a VL of SEQ ID NO: 247, a VH of SEQ ID NO:251 and a VL of SEQ ID NO: 255, a VH of SEQ ID NO:259 and a VL of SEQ ID NO: 263, and a VH of SEQ ID NO:267 and a VL of SEQ ID NO: 271.

25. A monoclonal antibody which binds to the same epitope of TDP-43 as an antibody selected from the group consisting of: NI-205.3F10, NI-205.51C1, NI-205.21G2, NI-205.8A2, NI-205.15F12, NI-205.113C4, NI-205.25F3, NI-205.87E7, NI-205.21G1, NI-205.68G5, NI-205.20A1, NI205.41D1, NI205.29E11, NI205.9E12, NI205.98H6,

NI205.10D3, NI205.44B2, NI205.38H2, NI205.36D5, NI205.58E11, NI205.14H5, NI205.31D2, NI205.8F8, NI205.31C11, NI205.8C10, NI205.10H7, NI205.1A9, NI205.14W3, and NI205.19G5.

26. A monoclonal antibody which competes for specific binding to TDP-43 with an antibody selected from the group consisting of: NI-205.3F10, NI-205.51C1, NI-205.21G2, NI-205.8A2, NI-205.15F12, NI-205.113C4, NI-205.25F3, NI-205.87E7, NI-205.21G1, NI-205.68G5, NI-205.20A1, NI205.41D1, NI205.29E11, NI205.9E12, NI205.98H6, NI205.10D3, NI205.44B2, NI205.38H2, NI205.36D5, NI205.58E11, NI205.14H5, NI205.31D2, NI205.8F8, NI205.31C11, NI205.8C10, NI205.10H7, NI205.1A9, NI205.14W3, and NI205.19G5.

27. The antibody of any one of claims 2 to 26, which is a human antibody, humanized antibody, chimeric antibody or murinized antibody.

28. The antibody of any one of claims 1 to 27, which is an antigen binding antibody fragment.

29. The antibody of claim 28, wherein the antibody fragment 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.

30. An isolated polypeptide comprising a VH and/or a VL of the antibody of any one of claims 10 to 29.

31. An isolated polynucleotide comprising a nucleotide sequence encoding the polypeptide of claim 30.

32. The polynucleotide of claim 31 comprising a nucleotide sequence selected from the group consisting of: SEQ ID NO: 95-116 and 275-310.

33. A vector comprising the polynucleotide of claims 31 or 32.

34. A host cell comprising the polynucleotide of claims 31 or 32 or the vector of claim 33.

35. A method for preparing an anti-TDP-43 antibody or immunoglobulin chain(s) thereof, said method comprising

(a) culturing the cell of claim 34; and

(b) isolating said antibody or immunoglobulin chain(s) thereof from the culture.

36. An antibody obtained by the method of claim 35.

37. The antibody of any one of claims 1 to 29 or 36, which is detectably labeled.

38. The antibody of claim 37, wherein the detectable label is selected from the group consisting of an enzyme, a radioisotope, a fluorophore and a heavy metal.

39. The antibody of any one of claims 1 to 29 or 36 to 38, which is attached to a drug.

40. A composition comprising the antibody of any one of claims 1 to 29 or 36 to 39.

41. The composition of claim 40, which is a pharmaceutical composition and further comprises a pharmaceutically acceptable carrier.

42. The composition of claim 41, which is a vaccine.

43. The pharmaceutical composition of claims 41 or 42 further comprising an additional agent useful for treating a TDP-43 proteinopathy.

44. The composition of claim 40, which is a diagnostic composition, and optionally comprises reagents conventionally used in immuno or nucleic acid based diagnostic methods.

45. A method of treating a TDP-43 proteinopathy in a subject in need thereof, comprising administering a therapeutically effective amount of the antibody of any one of claims 1 to 29 or 36 to 39.

46. Use of an antibody of any one of claims 1 to 29 or 36 to 39 for the preparation of a pharmaceutical or diagnostic composition for prophylactic and therapeutic treatment, monitoring the progression, or monitoring the response to a treatment of a TDP-43 proteinopathy in a subject.

47. A method of diagnosing a TDP-43 proteinopathy in a subject, the method comprising:

(a) assessing the level of TDP-43 in a sample from the subject to be diagnosed with antibody of any one of claims 1 to 29 or 36 to 398; and

(b) comparing the level of TDP-43 to a reference standard that indicates the level of the TDP-43 in one or more control subjects,

wherein a difference or similarity between the level of the TDP-43 and the reference standard indicates that the subject suffers from a TDP-43 proteinopathy.

48. The use of claim 46 or the method of claims 45 or 47, wherein the TDP-43 proteinopathy is selected from the group consisting of argyrophilic grain disease, Alzheimer's disease, amyotrophic lateral sclerosis (ALS), ALS-Parkinsonism dementia complex of Guam, corticobasal degeneration, Dementia with Lewy bodies, Huntington's disease, Lewy body disease, motor neuron disease, frontotemporal lobar degeneration (FTLD), frontotemporal dementia, frontotemporal lobar degeneration with ubiquitin-positive inclusions, hippocampal sclerosis, inclusion body myopathy, inclusion body myositis, Parkinson's disease, Parkinson's disease dementia, Parkinson-dementia complex in Kii peninsula and Pick's disease.

49. Use of the antibody of any one of claims 1 to 29 or 36 to 39 for the preparation of a composition for in vivo detection of or targeting a therapeutic and/or diagnostic agent to TDP-43 in the human or animal body.

50. The use of claim 49 wherein said in vivo imaging comprises positron emission tomography (PET), single photon emission tomography (SPECT), near infrared (NIR) optical imaging or magnetic resonance imaging (MRI).

51. A kit useful in the diagnosis or monitoring the progression of a TDP-43 proteinopathy, said kit comprising at least one antibody of any one of claims 1 to 29 or 36 to 39.

## CLAIMS

1. An invention not claimed in any divisional application.