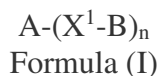


CLAIMS

WHAT IS CLAIMED IS:

1. An anti-transferrin receptor antibody comprising a variable heavy chain (VH) region and a variable light chain (VL) region, wherein the VH region comprises HCDR1 sequence comprising SEQ ID NO: 1; HCDR2 sequence comprising EINPIX₁GRSNYAX₂KFQG (SEQ ID NO: 88), wherein X₁ is selected from N or Q and X₂ is selected from Q or E; and HCDR3 sequence comprising SEQ ID NO: 3, and wherein the VL region comprises LCDR1 sequence comprising RTSENIYX₃NLA (SEQ ID NO: 89), LCDR2 sequence comprising AX₄TNLAX₅ (SEQ ID NO: 90), and LCDR3 sequence comprising QHFWGTPLTX₆ (SEQ ID NO: 91), wherein X₃ is selected from N or S, X₄ is selected from A or G, X₅ is selected from D or E, and X₆ is present or absent, and if present, is F.
2. The anti-transferrin receptor antibody of claim 1, wherein the VH region comprises HCDR1 sequence comprising SEQ ID NO: 1, HCDR2 sequence comprising SEQ ID NO: 4, and HCDR3 sequence comprising SEQ ID NO: 3.
3. The anti-transferrin receptor antibody of claim 1, wherein the V_L region comprises LCDR1 sequence comprising SEQ ID NO: 6, LCDR2 sequence comprising AATNLAX₅ (SEQ ID NO: 92), and LCDR3 sequence comprising QHFWGTPLTX₆ (SEQ ID NO: 91), wherein X₅ is selected from D or E and X₆ is present or absent, and if present, is F.
4. The anti-transferrin receptor antibody of claim 1, wherein the VL region comprises LCDR1 sequence comprising SEQ ID NO: 6, LCDR2 sequence comprising SEQ ID NO: 7, and LCDR3 sequence comprising SEQ ID NO: 8.
5. The anti-transferrin receptor antibody of claim 1, wherein the VH region comprises HCDR1 sequence comprising SEQ ID NO: 1, HCDR2 sequence comprising SEQ ID NO: 4, and HCDR3 sequence comprising SEQ ID NO: 3; and the VL region comprises LCDR1 sequence comprising SEQ ID NO: 6, LCDR2 sequence comprising SEQ ID NO: 7, and LCDR3 sequence comprising SEQ ID NO: 8.
6. The anti-transferrin receptor antibody of claim 1, wherein the VH region comprises at least 80%, 85%, 90%, 95%, 99%, or 100% sequence identity to a sequence selected from SEQ ID NOs: 13-16, and wherein the VL region comprises at least 80%, 85%, 90%, 95%, 99%, or 100% sequence identity to a sequence selected from SEQ ID NOs: 18-21.
7. The anti-transferrin receptor antibody of claim 1, wherein the anti-transferrin receptor antibody comprises a humanized antibody or binding fragment thereof or a chimeric antibody or binding fragment thereof.
8. The anti-transferrin receptor antibody of claim 1, wherein the anti-transferrin receptor antibody comprises a multi-specific antibody or a binding fragment thereof.

9. The anti-transferrin receptor antibody of claim 1, wherein the anti-transferrin receptor antibody comprises an IgG-scFv, nanobody, BiTE, diabody, DART, TandAb, scDiabody, scDiabody-CH3, triple body, mini-antibody, minibody, TriBi minibody, scFv-CH3 KIH, Fab-scFv-Fc KIH, Fab-scFv, scFv-CH-CL-scFv, Fab', F(ab')₂, F(ab')₃, F(ab')₂-scFv₂, scFv, scFv-KIH, Fab-scFv-Fc, tetravalent HCAb, scDiabody-Fc, diabody-Fc, tandem scFv-Fc, or intrabody.
10. The anti-transferrin receptor antibody of claim 1, wherein the anti-transferrin receptor antibody comprises at least one of an IgG1 framework, an IgG2 framework, an IgG2b framework, or an IgG4 framework.
11. The anti-transferrin receptor antibody of claim 1, wherein the anti-transferrin receptor antibody further comprises at least one mutation in the Fc region, and the at least one mutation modulates effector function.
12. The anti-transferrin receptor antibody of claim 11, wherein the effector function comprises attenuation or elimination of Fc-γ receptor binding.
13. The anti-transferrin receptor antibody of claim 11, wherein the at least one mutation is at residue position D265, N297, K322, L328, or P329, wherein the residue position is in reference to IgG1.
14. The anti-transferrin receptor antibody of claim 11, wherein the Fc region comprises mutations at L233 and L234, wherein the residues correspond to position 233 and 234 of SEQ ID NO: 23.
15. The anti-transferrin receptor antibody of claim 11, wherein the Fc region comprises mutations at D265 and N297.
16. The anti-transferrin receptor antibody of claim 1, wherein the anti-transferrin receptor antibody comprises a heavy chain (HC) sequence selected from SEQ ID NOs: 23-46 and a light chain (LC) sequence selected from SEQ ID NOs: 47-50.
17. The anti-transferrin receptor antibody of claim 1, wherein the anti-transferrin receptor antibody specifically binds to human transferrin receptor (TfR).
18. An anti-transferrin receptor antibody conjugate, comprising Formula (I):



wherein,

A comprises the anti-transferrin receptor antibody, wherein the anti-transferrin receptor antibody comprises a variable heavy chain (VH) region and a variable light chain (VL) region, wherein the VH region comprises HCDR1 sequence comprising SEQ ID NO: 1; HCDR2 sequence comprising EINPIX₁GRSNYAX₂KFQG (SEQ ID NO: 88), wherein X₁ is selected from N or Q

and X₂ is selected from Q or E; and HCDR3 sequence comprising SEQ ID NO: 3, and wherein the VL region comprises LCDR1 sequence comprising RTSENIYX₃NLA (SEQ ID NO: 89), LCDR2 sequence comprising AX₄TNLAX₅ (SEQ ID NO: 90), and LCDR3 sequence comprising QHFWGTPLTX₆ (SEQ ID NO: 91), wherein X₃ is selected from N or S, X₄ is selected from A or G, X₅ is selected from D or E, and X₆ is present or absence, and if present, is F; B comprises a polynucleic acid molecule; X¹ consists of a bond or linker; and n is an averaged value selected from 1-12.

19. The anti-transferrin receptor antibody conjugate of claim 18, wherein the polynucleic acid molecule comprises a passenger strand and a guide strand.

20. The anti-transferrin receptor antibody conjugate of claim 19, wherein the guide strand comprises at least one modified internucleotide linkage, at least one inverted abasic moiety, at least one 5'-vinylphosphonate modified non-natural nucleotide, or a combination thereof.

21. The anti-transferrin receptor antibody conjugate of claim 18, wherein the polynucleic acid molecule further comprises a modification of a sugar moiety at the 2' position, and wherein the modification at the 2'-position is selected from 2'-O-methyl, 2'-O-methoxyethyl (2'-O-MOE), 2'-deoxy, 2'-deoxy-2'-fluoro, 2'-O-aminopropyl (2'-O-AP), 2'-O-dimethylaminoethyl (2'-O-DMAOE), 2'-O-dimethylaminopropyl (2'-O-DMAP), 2'-O-dimethylaminoethoxyethyl (2'-O-DMAEOE), or 2'-O—N-methylacetamido (2'-O-NMA) modified nucleotide.

22. The anti-transferrin receptor antibody conjugate of claim 19, wherein the passenger strand comprises at least 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, or more phosphorodiamidate morpholino oligomer-modified non-natural nucleotides.

23. The anti-transferrin receptor antibody conjugate of claim 19, wherein A-X¹ is conjugated to the 5' end of the passenger strand or 3' end of the passenger strand.

24. The anti-transferrin receptor antibody conjugate of claim 18, wherein the polynucleic acid molecule hybridizes to a target sequence of a gene, and wherein the polynucleic acid molecule mediates RNA interference against the gene.

25. The anti-transferrin receptor antibody conjugate of claim 24, the gene comprises an upregulated gene within the IGF1-Akt-FoxO pathway, the glucocorticoids-GR pathway, the PGC1 α -FoxO pathway, the TNF α -NF κ B pathway, or the myostatin-ActRIIb-Smad2/3 pathway, E3 ligase, Forkhead box transcription factor, atrogin-1 gene (FBXO32), MuRF1 gene (TRIM63), FOXO1, FOXO3, MSTN, DMD, or DMPK.

26. The anti-transferrin receptor antibody conjugate of claim 24, wherein the RNA interference is preferentially mediated in a muscle when the anti-transferrin receptor antibody conjugate is administered to a subject.

27. A pharmaceutical composition comprising:

an anti-transferrin receptor antibody of claim 1; and
a pharmaceutically acceptable excipient.