

CLAIMS

What is claimed is:

1. An antibody that binds to human transferrin receptor (TfR), wherein the antibody comprises:
 - (i) a heavy chain complementary determining region 1 (CDR-H1), a heavy chain complementary determining region 2 (CDR-H2), and a heavy chain complementary determining region 3 (CDR-H3) of a heavy chain variable region (VH) comprising the amino acid sequence of SEQ ID NO: 15; and a light chain complementary determining region 1 (CDR-L1), a light chain complementary determining region 2 (CDR-L2), and a light chain complementary determining region 3 (CDR-L3) of a light chain variable region (VL) comprising the amino acid sequence of SEQ ID NO: 16;
 - (ii) a CDR-H1, a CDR-H2, and a CDR-H3 of a VH comprising the amino acid sequence of SEQ ID NO: 7; and CDR-L1, a CDR-L2, and CDR-L3 of a VL comprising the amino acid sequence of SEQ ID NO: 8; or
 - (iii) a CDR-H1, a CDR-H2, and a CDR-H3 of a VH comprising the amino acid sequence of SEQ ID NO: 23; and CDR-L1, a CDR-L2, and CDR-L3 of a VL comprising the amino acid sequence of SEQ ID NO: 24.
2. The antibody of claim 1, wherein the antibody comprises:
 - (i) a CDR-H1 as set forth in SEQ ID NO: 155, a CDR-H2 as set forth in SEQ ID NO: 156, a CDR-H3 as set forth in SEQ ID NO: 157; and a CDR-L1 as set forth in SEQ ID NO: 158, a CDR-L2 as set forth in SEQ ID NO: 159, and a CDR-L3 as set forth in SEQ ID NO: 14;
 - (ii) a CDR-H1 as set forth in SEQ ID NO: 145, a CDR-H2 as set forth in SEQ ID NO: 146, a CDR-H3 as set forth in SEQ ID NO: 147; and a CDR-L1 as set forth in SEQ ID NO: 148, a CDR-L2 as set forth in SEQ ID NO: 149, and a CDR-L3 as set forth in SEQ ID NO: 6; or
 - (iii) a CDR-H1 as set forth in SEQ ID NO: 165, a CDR-H2 as set forth in SEQ ID NO: 166, a CDR-H3 as set forth in SEQ ID NO: 167; and a CDR-L1 as set forth in SEQ ID NO: 168, a CDR-L2 as set forth in SEQ ID NO: 169, and a CDR-L3 as set forth in SEQ ID NO: 22.
3. The antibody of claim 1 or claim 2, wherein the antibody comprises human or humanized framework regions with:

- (i) the CDR-H1, the CDR-H2, the CDR-H3 of a VH as set forth in SEQ ID NO: 15, and the CDR-L1, the CDR-L2, the CDR-L3 of a VL as set forth in SEQ ID NO: 16;
 - (ii) the CDR-H1, the CDR-H2, the CDR-H3 of a VH as set forth in SEQ ID NO: 7, and the CDR-L1, the CDR-L2, the CDR-L3 of a VL as set forth in SEQ ID NO: 8; or
 - (iii) the CDR-H1, the CDR-H2, the CDR-H3 of a VH as set forth in SEQ ID NO: 23, and the CDR-L1, the CDR-L2, the CDR-L3 of a VL as set forth in SEQ ID NO: 24.
4. The antibody of any one of claims 1-3, wherein the antibody comprises:
- (i) a VH comprising an amino acid sequence at least 80% identical to SEQ ID NO: 15, and a VL comprising an amino acid sequence at least 80% identical to SEQ ID NO: 16;
 - (ii) a VH comprising an amino acid sequence at least 80% identical to SEQ ID NO: 7, and a VL comprising an amino acid sequence at least 80% identical to SEQ ID NO: 8; or
 - (iii) a VH comprising an amino acid sequence at least 80% identical to SEQ ID NO: 23, and a VL comprising an amino acid sequence at least 80% identical to SEQ ID NO: 24;
5. The antibody of any one of claims 1-4, wherein the antibody is selected from the group consisting of a full-length IgG, a Fab fragment, a F(ab') fragment, a F(ab')₂ fragment, a scFv, and a Fv.
6. The antibody of claim 5, wherein the antibody is a full-length IgG.
7. The antibody of claim 6, wherein the antibody comprises a heavy chain constant region of the isotype IgG1 set forth in SEQ ID NO: 175 or SEQ ID NO: 176.
8. The antibody of claim 6 or claim 7, wherein the antibody comprises:
- (i) a heavy chain comprising an amino acid sequence at least 80% identical to SEQ ID NO: 180, and a light chain comprising an amino acid sequence at least 80% identical to SEQ ID NO: 181;
 - (ii) a heavy chain comprising an amino acid sequence at least 80% identical to SEQ ID NO: 178, and a light chain comprising an amino acid sequence at least 80% identical to SEQ ID NO: 179; or
 - (iii) a heavy chain comprising an amino acid sequence at least 80% identical to SEQ ID NO: 182, and a light chain comprising an amino acid sequence at least 80% identical to SEQ ID NO: 183.
9. The antibody of claim 5, wherein the antibody is a F(ab') fragment.

10. The antibody of claim 9, wherein the antibody comprises:
- (i) a heavy chain comprising an amino acid sequence at least 85% identical to SEQ ID NO: 186, and a light chain comprising an amino acid sequence at least 85% identical to SEQ ID NO: 181;
 - (ii) a heavy chain comprising an amino acid sequence at least 85% identical to SEQ ID NO: 185, and a light chain comprising an amino acid sequence at least 85% identical to SEQ ID NO: 179; or
 - (iii) a heavy chain comprising an amino acid sequence at least 85% identical to SEQ ID NO: 187, and a light chain comprising an amino acid sequence at least 85% identical to SEQ ID NO: 183.
11. The antibody of any one of claims 1-10, wherein the antibody binds transferrin receptor 1 (TfR1) with a K_D of less than 10^{-8} M.
12. A nucleic acid encoding the antibody of any one of claims 1-11.
13. A method of producing an anti-TfR1 antibody, comprising culturing cells comprising the nucleic acid of claim 12 under conditions suitable for the expression of the antibody.
14. A complex comprising the antibody of any one of claims 1-11 covalently linked to a molecular payload, optionally wherein the antibody and the molecular payload are linked via a linker, optionally wherein the molecular payload is an oligonucleotide.
15. A method of detecting a transferrin receptor in a biological sample, comprising contacting the antibody of any one of claims 1-11 with the biological sample and measuring binding of the antibody to the biological sample, optionally wherein the antibody is covalently linked to a diagnostic agent.
16. A method of delivering a molecular payload to a cell, comprising contacting the cell with the complex of claim 14.
17. The method of claim 16, wherein the cell is a muscle cell.
18. A method of delivering a molecular payload to the brain or the muscle of a subject, comprising administering to the subject an effective amount of the complex of claim 14.
19. A method of treating a disease, comprising administering to the subject an effective amount of the complex of claim 14, wherein the molecular payload is a therapeutic agent.

20. The method of claim 19, wherein the disease is a neurological disease and the molecular payload is a drug for treating a neurological disease, or wherein the disease is a muscle disease and the molecular payload is a drug for treating a muscle disease, optionally wherein the muscle disease is a rare muscle disease or muscle atrophy.