

ANTI-TRANSFERRIN RECEPTOR ANTIBODIES AND USES THEREOF

CROSS-REFERENCE

[0001] This application claims the benefit of U.S. Provisional Application No. 62/784,181, filed December 21, 2018, which is incorporated herein by reference in its entirety.

BACKGROUND OF THE DISCLOSURE

[0002] The present invention is in the fields of pharmaceutical agents and ~~specieally~~specifically relates to antibody. This invention provides anti-transferrin receptor antibodies and ~~metheds~~methods of preparing and using the anti-transferrin receptor antibodies.

[0003] In addition to known uses in diagnostics, antibodies have been shown to be useful as therapeutic agents. For example, immunotherapy, or the use of antibodies for therapeutic purposes has been used in recent years to treat cancer and other disorders. The transferrin receptor is one of the mostly widely targeted receptors for development of targeted cancer diagnostics and therapeutics. This type II transmembrane glycoprotein is responsible for cellular iron transport and is found at low levels on the surface of many normal cell types. There is a need for developing improved anti-transferrin receptor antibody for ~~pharneeuteal~~pharmaceutical uses.

SUMMARY OF THE DISCLOSURE

[0003a] In one aspect, provided herein is 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.

[0003b] In one aspect, provided herein is anti-transferrin receptor antibody conjugate, comprising Formula (I):



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.

[0003c] In one aspect, provided herein is a pharmaceutical composition comprising: an anti-transferrin receptor antibody as described herein; and a pharmaceutically acceptable excipient.

[0004] Disclosed herein, in certain embodiments, are anti-transferrin receptor antibodies, anti-transferrin receptor antibody conjugates, and pharmaceutical compositions which comprise the anti-transferrin receptor antibodies or conjugates. In some embodiments, also disclosed herein are methods of delivering a payload utilizing an anti-transferrin receptor antibody described herein, and methods of treatment with use of an anti-transferrin receptor antibody described herein.

[0005] Disclosed herein, in certain embodiments, is 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 EINPIX₁GRSNYAX₂KFQG, wherein X₁ is selected from N or Q and X₂ is selected from Q or E; and HCDR3 sequence comprising SEQ ID NO: 3. In some embodiments, the VH region comprises HCDR1 sequence comprising SEQ ID NO: 1, HCDR2 sequence comprising SEQ ID NO: 2, and HCDR3 sequence comprising SEQ ID NO: 3. In some embodiments, 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. In some embodiments, the VH region comprises HCDR1 sequence comprising SEQ ID NO: 1, HCDR2 sequence comprising SEQ ID NO: 5, and HCDR3 sequence comprising SEQ ID NO: 3. In some embodiments, the VL region comprises LCDR1 sequence RTSENIYX₃NLA, LCDR2 sequence AX₄TNLAX₅, and LCDR3