

IMMUNOMODULATORY ANTIBODIES AND USES THEREOF

SEQUENCE LISTING

[0001] The instant application contains a Sequence Listing which has been submitted electronically in ASCII format and is hereby incorporated by reference in its entirety. Said ASCII copy, created on January 14, 2022, is named “ONR-006WO_SL.txt” and is 37,676 bytes in size.

CROSS-REFERENCE TO RELATED APPLICATIONS

[0002] This application claims the benefit of U.S. Provisional Patent Application No. 63/199,732, filed January 20, 2021, and U.S. Provisional Patent Application No. 63/200,897, filed April 1, 2021, both of which are incorporated by reference herein in their entirety.

SUMMARY OF THE DISCLOSURE

[0003] Provided herein are antibodies, including antigen-binding fragments and other antigen-binding polypeptides, that are useful in the treatment of cancer and fibrosis.

[0003a] Disclosed herein, in certain embodiments, is an antibody, comprising: (a) a light chain CDR1 sequence comprising the formula: RASQSISX8YLN (SEQ ID NO: 13), wherein X8 is S, R, K, or H; and (b) a light chain CDR2 sequence comprising the formula: AASSLQX9 (SEQ ID NO: 14), wherein X9 is S, N, Q, or T; and (c) a light chain CDR3 sequence comprising the formula: QQSYSTX10X11GX12 (SEQ ID NO: 15), wherein X10 is P, Q, T, S, N, A, or G; X11 is R, G, A, or S; and X12 is T, S, A, G, or N; and (d) a heavy chain CDR1 sequence comprising the formula: SX1X2MH (SEQ ID NO: 25), wherein X1 is Y, E, Q, or D; and X2 is A, D, T, V, S, G, or E; and (e) a heavy chain CDR2 sequence comprising the formula: VISX3DGSNKYX4ADSVKG (SEQ ID NO: 26), wherein X3 is Y, E, Q, or D; and X4 is Y, N, H, E, D, K, Q, or R; and (f) a heavy chain CDR3 sequence comprising the formula: ENVRPYYDFWX5GYX6SEYYYYGX7DV (SEQ ID NO: 27), wherein X5 is S, R, K, or H; X6 is Y, S, N, T, A, or Q; and X7 is M, L, I, or V; provided that the antibody does not comprise a sequence as set forth in SEQ ID NO: 1, SEQ ID NO: 2, and SEQ ID NO: 3.

[0003b] Disclosed herein, in certain embodiments, is an antibody, comprising: (a) a light chain CDR1 having an amino acid sequence 100% identical to an amino acid sequence set forth in the group consisting of: SEQ ID NO: 1, SEQ ID NO: 7, and SEQ ID NO: 13; a light chain CDR2 having an amino acid sequence 100% identical to an amino acid sequence set forth in the group consisting of: SEQ ID NO: 2, SEQ ID NO: 9, and SEQ ID NO: 14; and a light chain CDR3 having an amino acid sequence 100% identical to an amino acid sequence set forth in the group

consisting of: SEQ ID NO: 3, SEQ ID NO: 8, SEQ ID NO: 10, SEQ ID NO: 11, SEQ ID NO: 12, and SEQ ID NO: 15; and (b) a heavy chain CDR1 having an amino acid sequence 100% identical to an amino acid sequence set forth in the group consisting of: SEQ ID NO: 4, SEQ ID NO: 16, SEQ ID NO: 19, SEQ ID NO: 22 and SEQ ID NO: 25; a heavy chain CDR2 having an amino acid sequence 100% identical to an amino acid sequence set forth in the group consisting of: SEQ ID NO: 5, SEQ ID NO: 17, SEQ ID NO: 20, SEQ ID NO: 23, and SEQ ID NO: 26; a heavy chain CDR3 having an amino acid sequence 100%, identical to an amino acid sequence set forth in the group consisting of: SEQ ID NO: 6, SEQ ID NO: 18, SEQ ID NO: 21, SEQ ID NO: 24, and SEQ ID NO: 27; provided that the antibody does not comprise a sequence at least as set forth in SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, and SEQ ID NO: 6.

[0003c] Disclosed herein, in certain embodiments, is the use of an antibody as described herein in the manufacture of a medicament for the treatment of a cancer in a subject in need thereof, wherein the medicament is to be administered in a therapeutically effective amount to the subject.

[0003d] Disclosed herein, in certain embodiments, is the use of an antibody as described herein in the manufacture of a medicament for the treatment of a fibrotic disease or disorder associated with a presence of M2 macrophages in a subject in need thereof, wherein the medicament is to be administered in a therapeutically effective amount to the subject.

[0003e] Disclosed herein, in certain embodiments, is a pharmaceutical composition, comprising (a) an antibody as described herein, and (b) a pharmaceutically acceptable excipient.

[0003f] Disclosed herein, in certain embodiments, is the use of a composition as described herein in the manufacture of a medicament for the treatment of a cancer or a fibrotic disease in a subject.

[0003g] Disclosed herein, in certain embodiments, is an antibody as described herein and a pharmaceutical composition as described herein for use in therapy.

[0004] Disclosed herein, in certain embodiments, are antibodies, comprising: (a) a heavy chain variable region (VH) having a sequence at least 80% identical to an amino acid sequence selected from the group consisting of: SEQ ID NO: 29, SEQ ID NO: 31, SEQ ID NO: 33, SEQ ID NO: 35, SEQ ID NO: 37, SEQ ID NO: 39, and SEQ ID NO: 41; and (b) a light chain variable region (VL) having a sequence at least 80% identical to an amino acid sequence selected from the group consisting of: SEQ ID NO: 28, SEQ ID NO: 30, SEQ ID NO: 32, SEQ ID NO: 34, SEQ ID NO: 36, SEQ ID NO: 38, and SEQ ID NO: 40; provided that the antibody does not comprise a light chain variable region (VL) having a sequence as set forth in SEQ ID NO: 40 and a heavy chain variable region (VH) having a sequence as set forth in SEQ ID NO. 41. In some embodiments,

the light chain variable region (VL) has a sequence at least 85% identical to the amino acid sequence selected from the group consisting of: SEQ ID NO: 28, SEQ ID NO: 30, SEQ ID NO: 32, SEQ ID NO: 34, SEQ ID NO: 36, SEQ ID NO: 38, and SEQ ID NO: 40. In some embodiments, the light chain variable region (VL) has a sequence at least 90% identical to the amino acid sequence selected from the group consisting of: SEQ ID NO: 28, SEQ ID NO: 30, SEQ ID NO: 32, SEQ ID NO: 34, SEQ ID NO: 36, SEQ ID NO: 38, and SEQ ID NO: 40. In some embodiments, the light chain variable region (VL) has a sequence at least 95% identical to the amino acid sequence selected from the group consisting of: SEQ ID NO: 28, SEQ ID NO: 30, SEQ ID NO: 32, SEQ ID NO: 34, SEQ ID NO: 36, SEQ ID NO: 38, and SEQ ID NO: 40. In some embodiments, the light chain variable region (VL) has a sequence at least 99% identical to