

CLAIMS

1. An antibody or an antigen-binding fragment thereof, wherein the antibody or antigen-binding fragment thereof

(a) immunospecifically binds to a cell recombinantly expressing a first form of MUC16, which first form is glycosylated, and wherein the amino acid sequence of the first form is SEQ ID NO:133;

(b) lacks immunospecific binding to a cell recombinantly expressing a second form of MUC16, which second form is unglycosylated, and wherein the amino acid sequence of the second form is SEQ ID NO:139;

(c) inhibits matrigel invasion in vitro of cells recombinantly expressing said first form of MUC16; and

(d) immunospecifically binds to an epitope comprising N-glycosylated asparagine 1806 of SEQ ID NO:150.

2. The antibody or antigen-binding fragment thereof of claim 1, wherein (i) the cell recombinantly expressing the first form of MUC16 is a SKOV3 cell; (ii) the cell recombinantly expressing the second form of MUC16 is a SKOV3 cell; and (iii) the cells in step (c) are SKOV3 cells.

3. The antibody or antigen-binding fragment thereof of claim 1 or 2, wherein the antibody or antigen-binding fragment thereof immunospecifically binds to the amino acid sequence CTRNGTQLQNFTLDRSSV (SEQ ID NO:130), wherein amino acid residue number 4 (N4) and amino acid residue number 10 (N10) of CTRNGTQLQNFTLDRSSV (SEQ ID NO:130) are glycosylated.

4. The antibody or antigen-binding fragment thereof of any one of claims 1-3, wherein the antibody or antigen-binding fragment thereof immunospecifically binds to the amino acid sequence CGTQLQNFTLDRSSV (SEQ ID NO:131), wherein amino acid residue number 7 (N7) of CGTQLQNFTLDRSSV (SEQ ID NO:131) is glycosylated.

5. The antibody or antigen-binding fragment thereof of claim 3 or 4, wherein the glycosylation consists of an N-linked chitobiose.

6. The antibody or antigen-binding fragment thereof of any one of claims 1-5, wherein the antibody or antigen-binding fragment thereof inhibits growth of a tumor that expresses a glycosylated form of MUC16.

7. The antibody or antigen-binding fragment thereof of any one of claims 1-6, wherein the antibody is a monoclonal antibody.

8. The antibody or antigen-binding fragment thereof of any one of claims 1-7, wherein the antibody or antigen-binding fragment thereof lacks immunospecific binding to a cell recombinantly expressing a third form of MUC16, which third form is glycosylated, and wherein the amino acid sequence of the third form is SEQ ID NO: 139.

9. The antibody or antigen-binding fragment thereof of any one of claims 1-7, wherein the antibody or antigen-binding fragment thereof comprises a VH comprising the amino acid sequence of:

(I)

QVX₂₁LKESGPGX₂₂LQPSQTLSTCSFSGFSLX₂₃TX₂₄GMGVGWX₂₅RQX₂₆SGKGLE
WLAHIWWDDX₂₇DKYYX₂₈PALKSRLTISX₂₉X₃₀X₃₁SKNQVFLKIX₃₂NVX₃₃TADX₃₄ATY
YCX₃₅RIGTAQATDALDYWGQGTSVTVSS (SEQ ID NO:101), wherein X₂₁ is T or N,
X₂₂ is I or K, X₂₃ is N or S, X₂₄ is V or L, X₂₅ is S or I, X₂₆ is P or S, X₂₇ is E or absent,
X₂₈ is N or Y, X₂₉ is K or R, X₃₀ is A or D, X₃₁ is T or S, X₃₂ is V or A, X₃₃ is G or D, X₃₄
is T, I, or S, and X₃₅ is T, S, or A; or

(II) SEQ ID NO:81; or

(III) SEQ ID NO:1; or

(IV) SEQ ID NO:21; or

(V) SEQ ID NO:41; or

(VI) SEQ ID NO:61.

10. The antibody or antigen-binding fragment thereof of any one of claims 1-7, wherein the antibody or antigen-binding fragment thereof comprises a VL comprising the amino acid sequence of:

(I)

DIVMTQAAPSX₃₆X₃₇VTPGESVSISCRSSKSLX₃₈X₃₉SNGNTYLYWFLQRPQGQSPQRL
IYYMSNLASGVDPDRFSGRGSFTDLX₄₀ISRVEAX₄₁DVG VYYCMQX₄₂LEX₄₃PLTFG

GGTKLEIK (SEQ ID NO:102), wherein X₃₆ is I or V, X₃₇ is P or S, X₃₈ is R or L, X₃₉ is K or H, X₄₀ is R or K, X₄₁ is E or G, X₄₂ is S or G, and X₄₃ is Y or H; or

(II) SEQ ID NO:82; or

(III) SEQ ID NO:22; or

(IV) SEQ ID NO:42; or

(V) SEQ ID NO:2; or

(VI) SEQ ID NO:62.

11. The antibody or antigen-binding fragment thereof of any one of claims 1-7, wherein the antibody or antigen-binding fragment thereof comprises:

(a) (i) a VH comprising a VH CDR1 comprising the amino acid sequence TX1GMGVG (SEQ ID NO:103), wherein X1 is L or V; a VH CDR2 comprising the amino acid sequence HIWWDDX2DKYYX3PALKS (SEQ ID NO:104), wherein X2 is E or absent, and X3 is Y or N; and a VH CDR3 comprising the amino acid sequence IGTAQATDALDY (SEQ ID NO:105); and (ii) a VL comprising a VL CDR1 comprising the amino acid sequence RSSKSLX4X5SNGNTYLY (SEQ ID NO:106), wherein X4 is R or L, and X5 is K or H; a VL CDR2 comprising the amino acid sequence YMSNLAS (SEQ ID NO:107); and a VL CDR3 comprising the amino acid sequence MQX6LEX7PLT (SEQ ID NO:108), wherein X6 is G or S, and X7 is H or Y; or

(b) (i) a VH comprising a VH CDR1 comprising the amino acid sequence GFSLX8TX9GM (SEQ ID NO:109), wherein X8 is N or S, and wherein X9 is L or V; a VH CDR2 comprising the amino acid sequence WDDX10 (SEQ ID NO:110), wherein X10 is E or absent; and a VH CDR3 comprising the amino acid sequence GTAQATDALD (SEQ ID NO:111); and (ii) a VL comprising a VL CDR1 comprising the amino acid sequence SKSLX11X12SNGNTY (SEQ ID NO:112), wherein X11 is L or R, and X12 is H or K; a VL CDR2 comprising the amino acid sequence YMS (SEQ ID NO:113); and a VL CDR3 comprising the amino acid sequence X13LEX14PL (SEQ ID NO:114), wherein X13 is G or S, and X14 is H or Y; or

(c) (i) a VH CDR1 comprising the amino acid sequence GFSLX15TX16GMG (SEQ ID NO:115), wherein X15 is N or S, and X16 is V or L; a VH CDR2 comprising the amino acid sequence IWWDDX17DK (SEQ ID NO:116), wherein X17 is E or absent; and a VH CDR3 comprising the amino acid sequence X18RIGTAQATDALDY (SEQ ID NO:117),

wherein X18 is T, A, or S; and (ii) a VL comprising a VL CDR1 comprising the amino acid sequence KSLX19X20SNGNTY (SEQ ID NO:118), wherein X19 is V or L, and X20 is H or K; a VL CDR2 comprising the amino acid sequence YMS (SEQ ID NO:119); and a VL CDR3 comprising the amino acid sequence MQSLEYPLT (SEQ ID NO:120); or

(d) (i) a VH comprising a VH CDR1 comprising the amino acid sequence of SEQ ID NO:83, a VH CDR2 comprising the amino acid sequence of SEQ ID NO:84, and a VH CDR3 comprising the amino acid sequence of SEQ ID NO:85; and (ii) a VL comprising a VL CDR1 comprising the amino acid sequence of SEQ ID NO:86, a VL CDR2 comprising the amino acid sequence of SEQ ID NO:87, and a VL CDR3 comprising the amino acid sequence of SEQ ID NO:88; or

(e) (i) a VH comprising a VH CDR1 comprising the amino acid sequence of SEQ ID NO:89, a VH CDR2 comprising the amino acid sequence of SEQ ID NO:90, and a VH CDR3 comprising the amino acid sequence of SEQ ID NO:91; and (ii) a VL comprising a VL CDR1 comprising the amino acid sequence of SEQ ID NO:92, a VL CDR2 comprising the amino acid sequence of SEQ ID NO:93, and a VL CDR3 comprising the amino acid sequence of SEQ ID NO:94; or

(f) (i) a VH comprising a VH CDR1 comprising the amino acid sequence of SEQ ID NO:95, a VH CDR2 comprising the amino acid sequence of SEQ ID NO:96, and a VH CDR3 comprising the amino acid sequence of SEQ ID NO:97 and (ii) a VL comprising a VL CDR1 comprising the amino acid sequence of SEQ ID NO:98, a VL CDR2 comprising the amino acid sequence of SEQ ID NO:99, and a VL CDR3 comprising the amino acid sequence of SEQ ID NO:100; or

(g) (i) a VH comprising a VH CDR1 comprising the amino acid sequence of SEQ ID NO:23, a VH CDR2 comprising the amino acid sequence of SEQ ID NO:24, and a VH CDR3 comprising the amino acid sequence of SEQ ID NO:25; and (ii) a VL comprising a VL CDR1 comprising the amino acid sequence of SEQ ID NO:26, a VL CDR2 comprising the amino acid sequence of SEQ ID NO:27, and a VL CDR3 comprising the amino acid sequence of SEQ ID NO:28; or

(h) (i) a VH comprising a VH CDR1 comprising the amino acid sequence of SEQ ID NO:29, a VH CDR2 comprising the amino acid sequence of SEQ ID NO:30, and a VH CDR3 comprising the amino acid sequence of SEQ ID NO:31; and (ii) a VL comprising a VL CDR1 comprising the amino acid sequence of SEQ ID NO:32, a VL CDR2 comprising the amino acid sequence of SEQ ID NO:33, and a VL CDR3 comprising the amino acid sequence of SEQ ID NO:34; or

(i) (i) a VH comprising a VH CDR1 comprising the amino acid sequence of SEQ ID NO:35, a VH CDR2 comprising the amino acid sequence of SEQ ID NO:36, and a VH CDR3 comprising the amino acid sequence of SEQ ID NO:37; and (ii) a VL comprising a VL CDR1

comprising the amino acid sequence of SEQ ID NO:38, a VL CDR2 comprising the amino acid sequence of SEQ ID NO:39, and a VL CDR3 comprising the amino acid sequence of SEQ ID NO:40; or

(j) (i) a VH comprising a VH CDR1 comprising the amino acid sequence of SEQ ID NO:43, a VH CDR2 comprising the amino acid sequence of SEQ ID NO:44, and a VH CDR3 comprising the amino acid sequence of SEQ ID NO:45; and (ii) a VL comprising a VL CDR1 comprising the amino acid sequence of SEQ ID NO:46, a VL CDR2 comprising the amino acid sequence of SEQ ID NO:47, and a VL CDR3 comprising the amino acid sequence of SEQ ID NO:48; or

(k) (i) a VH comprising a VH CDR1 comprising the amino acid sequence of SEQ ID NO:49, a VH CDR2 comprising the amino acid sequence of SEQ ID NO:50, and a VH CDR3 comprising the amino acid sequence of SEQ ID NO:51; and (ii) a VL comprising a VL CDR1 comprising the amino acid sequence of SEQ ID NO:52, a VL CDR2 comprising the amino acid sequence of SEQ ID NO:53, and a VL CDR3 comprising the amino acid sequence of SEQ ID NO:54; or

(l) (i) a VH comprising a VH CDR1 comprising the amino acid sequence of SEQ ID NO:55, a VH CDR2 comprising the amino acid sequence of SEQ ID NO:56, and a VH CDR3 comprising the amino acid sequence of SEQ ID NO:57; and (ii) a VL comprising a VL CDR1 comprising the amino acid sequence of SEQ ID NO:58, a VL CDR2 comprising the amino acid sequence of SEQ ID NO:59, and a VL CDR3 comprising the amino acid sequence of SEQ ID NO:60; or

(m) (i) a VH comprising a VH CDR1 comprising the amino acid sequence of SEQ ID NO:3, a VH CDR2 comprising the amino acid sequence of SEQ ID NO:4, and a VH CDR3 comprising the amino acid sequence of SEQ ID NO:5; and (ii) a VL comprising a VL CDR1 comprising the amino acid sequence of SEQ ID NO:6, a VL CDR2 comprising the amino acid sequence of SEQ ID NO:7, and a VL CDR3 comprising the amino acid sequence of SEQ ID NO:8; or

(n) (i) a VH comprising a VH CDR1 comprising the amino acid sequence of SEQ ID NO:9, a VH CDR2 comprising the amino acid sequence of SEQ ID NO:10, and a VH CDR3 comprising the amino acid sequence of SEQ ID NO:11; and (ii) a VL comprising a VL CDR1 comprising the amino acid sequence of SEQ ID NO:12, a VL CDR2 comprising the amino acid sequence of SEQ ID NO:13, and a VL CDR3 comprising the amino acid sequence of SEQ ID NO:14; or

(o) (i) a VH comprising a VH CDR1 comprising the amino acid sequence of SEQ ID NO:15, a VH CDR2 comprising the amino acid sequence of SEQ ID NO:16, and a VH CDR3 comprising the amino acid sequence of SEQ ID NO:17; and (ii) a VL comprising a VL CDR1 comprising the amino acid sequence of SEQ ID NO:18, a VL CDR2 comprising the amino

acid sequence of SEQ ID NO:19, and a VL CDR3 comprising the amino acid sequence of SEQ ID NO:20; or

(p) (i) a VH comprising a VH CDR1 comprising the amino acid sequence of SEQ ID NO:63, a VH CDR2 comprising the amino acid sequence of SEQ ID NO:64, and a VH CDR3 comprising the amino acid sequence of SEQ ID NO:65; and (ii) a VL comprising a VL CDR1 comprising the amino acid sequence of SEQ ID NO:66, a VL CDR2 comprising the amino acid sequence of SEQ ID NO:67, and a VL CDR3 comprising the amino acid sequence of SEQ ID NO:68; or

(q) (i) a VH comprising a VH CDR1 comprising the amino acid sequence of SEQ ID NO:69, a VH CDR2 comprising the amino acid sequence of SEQ ID NO:70, and a VH CDR3 comprising the amino acid sequence of SEQ ID NO:71; and (ii) a VL comprising a VL CDR1 comprising the amino acid sequence of SEQ ID NO:72, a VL CDR2 comprising the amino acid sequence of SEQ ID NO:73, and a VL CDR3 comprising the amino acid sequence of SEQ ID NO:74; or

(r) (i) a VH comprising a VH CDR1 comprising the amino acid sequence of SEQ ID NO:75, a VH CDR2 comprising the amino acid sequence of SEQ ID NO:76, and a VH CDR3 comprising the amino acid sequence of SEQ ID NO:77; and (ii) a VL comprising a VL CDR1 comprising the amino acid sequence of SEQ ID NO:78, a VL CDR2 comprising the amino acid sequence of SEQ ID NO:79, and a VL CDR3 comprising the amino acid sequence of SEQ ID NO:80.

12. An antibody or antigen-binding fragment thereof of claim 1 that immunospecifically binds to MUC16, wherein the antibody or antigen-binding fragment thereof comprises a VH, which VH comprises:

(a) a VH CDR1 comprising the amino acid sequence TX1GMGVG (SEQ ID NO:103), wherein X1 is L or V; a VH CDR2 comprising the amino acid sequence HIWWDDX2DKYYX3PALKS (SEQ ID NO:104), wherein X2 is E or absent, and X3 is Y or N; and a VH CDR3 comprising the amino acid sequence IGTAQATDALDY (SEQ ID NO:105); or

(b) a VH CDR1 comprising the amino acid sequence GFSLX8TX9GM (SEQ ID NO:109), wherein X8 is N or S, and wherein X9 is L or V; a VH CDR2 comprising the amino acid sequence WDDX10 (SEQ ID NO:110), wherein X10 is E or absent; and a VH CDR3 comprising the amino acid sequence GTAQATDALD (SEQ ID NO:111); or

(c) a VH CDR1 comprising the amino acid sequence GFSLX15TX16GMG (SEQ ID NO:115), wherein X15 is N or S, and X16 is V or L; a VH CDR2 comprising the amino acid sequence IWWDDX17DK (SEQ ID NO:116), wherein X17 is E or absent; and a VH CDR3

comprising the amino acid sequence X18RIGTAQATDALDY (SEQ ID NO:117), wherein X18 is T, A, or S; or

(d) a VH CDR1 comprising the amino acid sequence of SEQ ID NO:83, a VH CDR2 comprising the amino acid sequence of SEQ ID NO:84, and a VH CDR3 comprising the amino acid sequence of SEQ ID NO:85; or

(e) a VH CDR1 comprising the amino acid sequence of SEQ ID NO:89, a VH CDR2 comprising the amino acid sequence of SEQ ID NO:90, and a VH CDR3 comprising the amino acid sequence of SEQ ID NO:91; or

(f) a VH CDR1 comprising the amino acid sequence of SEQ ID NO:95, a VH CDR2 comprising the amino acid sequence of SEQ ID NO:96, and a VH CDR3 comprising the amino acid sequence of SEQ ID NO:97; or

(g) a VH CDR1 comprising the amino acid sequence of SEQ ID NO:3, a VH CDR2 comprising the amino acid sequence of SEQ ID NO:4, and a VH CDR3 comprising the amino acid sequence of SEQ ID NO:5; or

(h) a VH CDR1 comprising the amino acid sequence of SEQ ID NO:9, a VH CDR2 comprising the amino acid sequence of SEQ ID NO:10, and a VH CDR3 comprising the amino acid sequence of SEQ ID NO:11; or

(i) a VH CDR1 comprising the amino acid sequence of SEQ ID NO:15, a VH CDR2 comprising the amino acid sequence of SEQ ID NO:16, and a VH CDR3 comprising the amino acid sequence of SEQ ID NO:17; or

(j) a VH CDR1 comprising the amino acid sequence of SEQ ID NO:23, a VH CDR2 comprising the amino acid sequence of SEQ ID NO:24, and a VH CDR3 comprising the amino acid sequence of SEQ ID NO:25; or

(k) a VH CDR1 comprising the amino acid sequence of SEQ ID NO:29, a VH CDR2 comprising the amino acid sequence of SEQ ID NO:30, and a VH CDR3 comprising the amino acid sequence of SEQ ID NO:31; or

(l) a VH CDR1 comprising the amino acid sequence of SEQ ID NO:35, a VH CDR2 comprising the amino acid sequence of SEQ ID NO:36, and a VH CDR3 comprising the amino acid sequence of SEQ ID NO:37; or

(m) a VH CDR1 comprising the amino acid sequence of SEQ ID NO:43, a VH CDR2 comprising the amino acid sequence of SEQ ID NO:44, and a VH CDR3 comprising the amino acid sequence of SEQ ID NO:45; or

(n) a VH CDR1 comprising the amino acid sequence of SEQ ID NO:49, a VH CDR2 comprising the amino acid sequence of SEQ ID NO:50, and a VH CDR3 comprising the amino acid sequence of SEQ ID NO:51; or

(o) a VH CDR1 comprising the amino acid sequence of SEQ ID NO:55, a VH CDR2 comprising the amino acid sequence of SEQ ID NO:56, and a VH CDR3 comprising the amino acid sequence of SEQ ID NO:57; or

(p) a VH CDR1 comprising the amino acid sequence of SEQ ID NO:63, a VH CDR2 comprising the amino acid sequence of SEQ ID NO:64, and a VH CDR3 comprising the amino acid sequence of SEQ ID NO:65; or

(q) a VH CDR1 comprising the amino acid sequence of SEQ ID NO:69, a VH CDR2 comprising the amino acid sequence of SEQ ID NO:70, and a VH CDR3 comprising the amino acid sequence of SEQ ID NO:71; or

(r) a VH CDR1 comprising the amino acid sequence of SEQ ID NO:75, a VH CDR2 comprising the amino acid sequence of SEQ ID NO:76, and a VH CDR3 comprising the amino acid sequence of SEQ ID NO:77.

13. An antibody or antigen-binding fragment thereof that immunospecifically binds to MUC16, wherein the antibody or antigen-binding fragment thereof comprises:

(a) (i) a VH comprising: a VH CDR1 comprising the amino acid sequence TX1GMGVG (SEQ ID NO:103), wherein X1 is L or V; a VH CDR2 comprising the amino acid sequence HIWWDDX2DKYYX3PALKS (SEQ ID NO:104), wherein X2 is E or absent, and X3 is Y or N; and a VH CD3 comprising the amino acid sequence IGTAQATDALDY (SEQ ID NO:105); and (ii) a VL comprising: a VL CDR1 comprising the amino acid sequence RSSKSLX4X5SNGNTYLY (SEQ ID NO:106), wherein X4 is R or L, and X5 is K or H; a VL CDR2 comprising the amino acid sequence YMSNLAS (SEQ ID NO:107); and a VL CDR3 comprising the amino acid sequence MQX6LEX7PLT (SEQ ID NO:108), wherein X6 is G or S, and X7 is H or Y; or

(b) (i) a VH comprising: a VH CDR1 comprising the amino acid sequence GFSLX8TX9GM (SEQ ID NO:109), wherein X8 is N or S, and wherein X9 is L or V; a VH CDR2 comprising the amino acid sequence WDDX10 (SEQ ID NO:110), wherein X10 is E or absent; and a VH CDR3 comprising the amino acid sequence GTAQATDALD (SEQ ID NO:111); and (ii) a VL comprising: a VL CDR1 comprising the amino acid sequence SKSLX11X12SNGNTY (SEQ ID NO:112), wherein X11 is L or R, and X12 is H or K; a VL CDR2 comprising the amino acid sequence YMS (SEQ ID NO:113); and a VL CDR3 comprising the amino acid sequence X13LEX14PL (SEQ ID NO:114), wherein X13 is G or S, and X14 is H or Y; or

(c) (i) a VH comprising: a VH CDR1 comprising the amino acid sequence GFSLX15TX16GMG (SEQ ID NO:115), wherein X15 is N or S, and X16 is V or L; a VH CDR2 comprising the amino acid sequence IWWDDX17DK (SEQ ID NO:116), wherein X17 is E or absent; and a VH CDR3 comprising the amino acid sequence X18RIGTAQATDALDY

(SEQ ID NO:117), wherein X18 is T, A, or S; and (ii) a VL comprising: a VL CDR1 comprising the amino acid sequence KSLX19X20SNGNTY (SEQ ID NO:118), wherein X19 is V or L, and X20 is H or K; a VL CDR2 comprising the amino acid sequence YMS (SEQ ID NO:119); and a VL CDR3 comprising the amino acid sequence MQSLEYPLT (SEQ ID NO:120).

14. An antibody or antigen-binding fragment thereof that immunospecifically binds to MUC16, wherein the antibody or antigen-binding fragment thereof comprises:

(a) (i) a VH comprising a VH CDR1 comprising the amino acid sequence of SEQ ID NO:83, a VH CDR2 comprising the amino acid sequence of SEQ ID NO:84, and a VH CDR3 comprising the amino acid sequence of SEQ ID NO:85; and (ii) a VL comprising a VL CDR1 comprising the amino acid sequence of SEQ ID NO:86, a VL CDR2 comprising the amino acid sequence of SEQ ID NO:87, and a VL CDR3 comprising the amino acid sequence of SEQ ID NO:88; or

(b) (i) a VH comprising a VH CDR1 comprising the amino acid sequence of SEQ ID NO:89, a VH CDR2 comprising the amino acid sequence of SEQ ID NO:90, and a VH CDR3 comprising the amino acid sequence of SEQ ID NO:91; and (ii) a VL comprising a VL CDR1 comprising the amino acid sequence of SEQ ID NO:92, a VL CDR2 comprising the amino acid sequence of SEQ ID NO:93, and a VL CDR3 comprising the amino acid sequence of SEQ ID NO:94; or

(c) (i) a VH comprising a VH CDR1 comprising the amino acid sequence of SEQ ID NO:95, a VH CDR2 comprising the amino acid sequence of SEQ ID NO:96, and a VH CDR3 comprising the amino acid sequence of SEQ ID NO:97; and (ii) a VL comprising a VL CDR1 comprising the amino acid sequence of SEQ ID NO:98, a VL CDR2 comprising the amino acid sequence of SEQ ID NO:99, and a VL CDR3 comprising the amino acid sequence of SEQ ID NO:100.

15. An antibody or antigen-binding fragment thereof that immunospecifically binds to MUC16, wherein the antibody or antigen-binding fragment thereof comprises:

(a) (i) a VH comprising a VH CDR1 comprising the amino acid sequence of SEQ ID NO:23, a VH CDR2 comprising the amino acid sequence of SEQ ID NO:24, and a VH CDR3 comprising the amino acid sequence of SEQ ID NO:25; and (ii) a VL comprising a VL CDR1 comprising the amino acid sequence of SEQ ID NO:26, a VL CDR2 comprising the amino acid sequence of SEQ ID NO:27, and a VL CDR3 comprising the amino acid sequence of SEQ ID NO:28; or

(b) (i) a VH comprising a VH CDR1 comprising the amino acid sequence of SEQ ID NO:29, a VH CDR2 comprising the amino acid sequence of SEQ ID NO:30, and a VH CDR3 comprising the amino acid sequence of SEQ ID NO:31; and (ii) a VL comprising a VL CDR1 comprising the amino acid sequence of SEQ ID NO:32, a VL CDR2 comprising the amino acid sequence of SEQ ID NO:33, and a VL CDR3 comprising the amino acid sequence of SEQ ID NO:34; or

(c) (i) a VH comprising a VH CDR1 comprising the amino acid sequence of SEQ ID NO:35, a VH CDR2 comprising the amino acid sequence of SEQ ID NO:36, and a VH CDR3 comprising the amino acid sequence of SEQ ID NO:37; and (ii) a VL comprising a VL CDR1 comprising the amino acid sequence of SEQ ID NO:38, a VL CDR2 comprising the amino acid sequence of SEQ ID NO:39, and a VL CDR3 comprising the amino acid sequence of SEQ ID NO:40.

16. An antibody or antigen-binding fragment thereof that immunospecifically binds to MUC16, wherein the antibody or antigen-binding fragment thereof comprises:

(a) (i) a VH comprising a VH CDR1 comprising the amino acid sequence of SEQ ID NO:43, a VH CDR2 comprising the amino acid sequence of SEQ ID NO:44, and a VH CDR3 comprising the amino acid sequence of SEQ ID NO:45; and (ii) a VL comprising a VL CDR1 comprising the amino acid sequence of SEQ ID NO:46, a VL CDR2 comprising the amino acid sequence of SEQ ID NO:47, and a VL CDR3 comprising the amino acid sequence of SEQ ID NO:48; or

(b) (i) a VH comprising a VH CDR1 comprising the amino acid sequence of SEQ ID NO:49, a VH CDR2 comprising the amino acid sequence of SEQ ID NO:50, and a VH CDR3 comprising the amino acid sequence of SEQ ID NO:51; and (ii) a VL comprising a VL CDR1 comprising the amino acid sequence of SEQ ID NO:52, a VL CDR2 comprising the amino acid sequence of SEQ ID NO:53, and a VL CDR3 comprising the amino acid sequence of SEQ ID NO:54; or

(c) (i) a VH comprising a VH CDR1 comprising the amino acid sequence of SEQ ID NO:55, a VH CDR2 comprising the amino acid sequence of SEQ ID NO:56, and a VH CDR3 comprising the amino acid sequence of SEQ ID NO:57; and (ii) a VL comprising a VL CDR1 comprising the amino acid sequence of SEQ ID NO:58, a VL CDR2 comprising the amino acid sequence of SEQ ID NO:59, and a VL CDR3 comprising the amino acid sequence of SEQ ID NO:60.

17. An antibody or antigen-binding fragment thereof that immunospecifically binds to MUC16, wherein the antibody or antigen-binding fragment thereof comprises:

(a) (i) a VH comprising a VH CDR1 comprising the amino acid sequence of SEQ ID NO:3, a VH CDR2 comprising the amino acid sequence of SEQ ID NO:4, and a VH CDR3 comprising the amino acid sequence of SEQ ID NO:5; and (ii) a VL comprising a VL CDR1 comprising the amino acid sequence of SEQ ID NO:6, a VL CDR2 comprising the amino acid sequence of SEQ ID NO:7, and a VL CDR3 comprising the amino acid sequence of SEQ ID NO:8; or

(b) (i) a VH comprising a VH CDR1 comprising the amino acid sequence of SEQ ID NO:9, a VH CDR2 comprising the amino acid sequence of SEQ ID NO:10, and a VH CDR3 comprising the amino acid sequence of SEQ ID NO:11; and (ii) a VL comprising a VL CDR1 comprising the amino acid sequence of SEQ ID NO:12, a VL CDR2 comprising the amino acid sequence of SEQ ID NO:13, and a VL CDR3 comprising the amino acid sequence of SEQ ID NO:14; or

(c) (i) a VH comprising a VH CDR1 comprising the amino acid sequence of SEQ ID NO:15, a VH CDR2 comprising the amino acid sequence of SEQ ID NO:16, and a VH CDR3 comprising the amino acid sequence of SEQ ID NO:17; and (ii) a VL comprising a VL CDR1 comprising the amino acid sequence of SEQ ID NO:18, a VL CDR2 comprising the amino acid sequence of SEQ ID NO:19, and a VL CDR3 comprising the amino acid sequence of SEQ ID NO:20.

18. An antibody or antigen-binding fragment thereof that immunospecifically binds to MUC16, wherein the antibody or antigen-binding fragment thereof comprises:

(a) (i) a VH comprising a VH CDR1 comprising the amino acid sequence of SEQ ID NO:63, a VH CDR2 comprising the amino acid sequence of SEQ ID NO:64, and a VH CDR3 comprising the amino acid sequence of SEQ ID NO:65; and (ii) a VL comprising a VL CDR1 comprising the amino acid sequence of SEQ ID NO:66, a VL CDR2 comprising the amino acid sequence of SEQ ID NO:67, and a VL CDR3 comprising the amino acid sequence of SEQ ID NO:68; or

(b) (i) a VH comprising a VH CDR1 comprising the amino acid sequence of SEQ ID NO:69, a VH CDR2 comprising the amino acid sequence of SEQ ID NO:70, and a VH CDR3 comprising the amino acid sequence of SEQ ID NO:71; and (ii) a VL comprising a VL CDR1 comprising the amino acid sequence of SEQ ID NO:72, a VL CDR2 comprising the amino acid sequence of SEQ ID NO:73, and a VL CDR3 comprising the amino acid sequence of SEQ ID NO:74; or

(c) (i) a VH comprising a VH CDR1 comprising the amino acid sequence of SEQ ID NO:75, a VH CDR2 comprising the amino acid sequence of SEQ ID NO:76, and a VH CDR3 comprising the amino acid sequence of SEQ ID NO:77; and (ii) a VL comprising a VL CDR1

comprising the amino acid sequence of SEQ ID NO:78, a VL CDR2 comprising the amino acid sequence of SEQ ID NO:79, and a VL CDR3 comprising the amino acid sequence of SEQ ID NO:80.

19. An antibody or antigen-binding fragment thereof that immunospecifically binds to MUC16, wherein the antibody or antigen-binding fragment thereof comprises:

(a) (i) a VH comprising the amino acid sequence of QVX₂₁LKESGPGX₂₂LQPSQTLSTCSFSGFSLX₂₃TX₂₄GMGVGWX₂₅RQX₂₆SGKGLEWLAHIWWDDX₂₇DKYYX₂₈PALKSRLTISX₂₉X₃₀X₃₁SKNQVFLKIX₃₂NVX₃₃TADX₃₄ATYYCX₃₅RIGTAQATDALDYWGQGTSVTVSS (SEQ ID NO:101), wherein X₂₁ is T or N, X₂₂ is I or K, X₂₃ is N or S, X₂₄ is V or L, X₂₅ is S or I, X₂₆ is P or S, X₂₇ is E or absent, X₂₈ is N or Y, X₂₉ is K or R, X₃₀ is A or D, X₃₁ is T or S, X₃₂ is V or A, X₃₃ is G or D, X₃₄ is T, I, or S, and X₃₅ is T, S, or A; and (ii) a VL comprising the amino acid sequence of DIVMTQAAPSX₃₆X₃₇VTPGESVSISCRSSKSLX₃₈X₃₉SNGNTYLYWFLQRPQGQSPQRLIYYMSNLASGVDPDRFSGRSGTGDTFTLX₄₀ISRVEAX₄₁DVGVIYCMQX₄₂LEX₄₃PLTFGGGKLEIK (SEQ ID NO:102), wherein X₃₆ is I or V, X₃₇ is P or S, X₃₈ is R or L, X₃₉ is K or H, X₄₀ is R or K, X₄₁ is E or G, X₄₂ is S or G, and X₄₃ is Y or H; or

(b) (i) a VH comprising the amino acid sequence of SEQ ID NO:81; and (ii) a VL comprising the amino acid sequence of SEQ ID NO:82; or

(c) (i) a VH comprising the amino acid sequence of SEQ ID NO:1; and (ii) a VL comprising the amino acid sequence of SEQ ID NO:2;

(d) (i) a VH comprising the amino acid sequence of SEQ ID NO:21; and (ii) a VL comprising the amino acid sequence of SEQ ID NO:22; or

(e) (i) a VH comprising the amino acid sequence of SEQ ID NO:41; and (ii) a VL comprising the amino acid sequence of SEQ ID NO:42; or

(f) (i) a VH comprising the amino acid sequence of SEQ ID NO:61; and (ii) a VL comprising the amino acid sequence of SEQ ID NO:62.

20. An antibody or antigen-binding fragment thereof that immunospecifically binds to MUC16, wherein the antibody or antigen-binding fragment thereof comprises: (i) a VH comprising the amino acid sequence of SEQ ID NO:81; and (ii) a VL comprising the amino acid sequence of SEQ ID NO:82.

21. The antibody or antigen-binding fragment thereof of any one of claims 1-8 and 11-18 wherein the antibody or antigen-binding fragment thereof is humanized.

22. The antibody or antigen-binding fragment thereof of any one of claims 1-21, wherein the antibody is a monoclonal antibody.

23. An antibody conjugate comprising the antibody or antigen-binding fragment thereof of any one of claims 1-22 conjugated to an agent.

24. The antibody or antigen-binding fragment thereof of any one of claims 1-22, wherein the antibody or antigen-binding fragment thereof is a bispecific antibody.

25. The bispecific antibody of claim 24, wherein the bispecific antibody comprises an immunoglobulin that immunospecifically binds MUC16, wherein the light chain of the immunoglobulin is conjugated via a peptide linker to a single chain variable fragment (scFv) that immunospecifically binds to CD3.

26. A bispecific antibody conjugate comprising the bispecific antibody of claim 24 or 25 conjugated to an agent.

27. The antibody or antigen-binding fragment thereof of any one of claims 1-22, which is an antigen-binding fragment that is a scFv.

28. A scFv conjugate comprising the scFv of claim 27 conjugated to an agent.

29. A chimeric antigen receptor (CAR) comprising: the scFv of claim 27 or the scFv conjugate of claim 31.

30. A CAR comprising the antigen-binding fragment of any one of claims 1-22.

31. A T cell which recombinantly expresses the CAR of claim 29 or 30.

32. A polynucleotide comprising nucleic acid sequences encoding: (i) the scFv of claim 27, (ii) the scFv conjugate of claim 28, or (iii) the CAR of claim 29 or 30.

33. An *ex vivo* cell comprising one or more polynucleotides encoding the antibody or antigen-binding fragment thereof of any one of claims 1-22 operably linked to a promoter.

34. A pharmaceutical composition comprising: a therapeutically effective amount of the antibody or antigen-binding fragment thereof of any one of claims 1-22, the antibody

conjugate of claim 23, the bispecific antibody of claim 24 or 25, the bispecific antibody conjugate of claim 26, the scFv of claim 27, the scFv conjugate of claim 28, or the CAR of claim 29.

35. A pharmaceutical composition comprising a therapeutically effective amount of the CAR of claim 30 and a pharmaceutically acceptable carrier.

36. A pharmaceutical composition comprising a therapeutically effective amount of the T cell of claim 31 and a pharmaceutically acceptable carrier.

37. The pharmaceutical composition of claim 34 for use in the treatment of cancer in a patient in need thereof.

38. The pharmaceutical composition of claim 35 for use in the treatment of cancer in a patient in need thereof.

39. The pharmaceutical composition of claim 36 for use in the treatment of cancer in a patient in need thereof.

40. The pharmaceutical composition of any one of claims 37-39, wherein said cancer is a cancer of the lung, pancreas, breast, uterine, fallopian tube, primary peritoneum, or ovary.

41. The pharmaceutical composition of any one of claims 37-40, wherein said patient is a human patient.

42. The pharmaceutical composition of any one of claims 37-41, wherein the pharmaceutical composition is to be administered to the patient in combination with a therapeutically effective amount of an additional therapeutic agent.