

Claims

1. An antigen binding protein that specifically recognizes a target Melanoma-Associated Antigen A4 (MAGE-A4) peptide-MHC (pMHC), comprising:
 - (a) an antibody heavy chain variable (VH) domain comprising an HCDR1 amino acid sequence of SNYAMS (SEQ ID NO: 469), an HCDR2 amino acid sequence of IVSSGGTTYADSVKG (SEQ ID NO: 657), and an HCDR3 amino acid sequence of DLYYGPSTYFVANL (SEQ ID NO: 731); and
 - (b) an antibody light chain variable (VL) domain comprising an LCDR1 amino acid sequence of TADTLRSYAS (SEQ ID NO: 472), an LCDR2 amino acid sequence of RDTSRPS (SEQ ID NO: 473), and an LCDR3 amino acid sequence of ATRPSSGSNFQL (SEQ ID NO: 879).
2. The antigen binding protein of claim 1, comprising:
 - (a) an antibody heavy chain variable (VH) domain comprising a framework region, an HCDR1 region, an HCDR2 region, and an HCDR3 region, wherein the VH domain comprises an amino acid sequence set forth in SEQ ID NO: 583, or an amino acid sequence with at least 80% identity to the framework region of the amino acid sequence set forth in SEQ ID NO: 583 and 100% identity to the HCDR1 region, HCDR2 region, and HCDR3 region set forth in SEQ ID NO: 583; and
 - (b) an antibody light chain variable (VL) domain comprising a framework region, an LCDR1 region, an LCDR2 region, and an LCDR3 region, wherein the VL domain comprises an amino acid sequence set forth in SEQ ID NO: 805, or an amino acid sequence with at least 80% identity to the framework region of the amino acid sequence set forth in SEQ ID NO: 805 and 100% identity to the LCDR1 region, LCDR2 region, and LCDR3 region set forth in SEQ ID NO: 805;
3. The antigen binding protein of claim 1, wherein the antigen binding protein is a humanized antigen binding protein
4. A bispecific antigen binding protein, comprising at least a first antigen binding domain comprising the antigen binding protein of claim 1, and at least a second antigen binding domain with specificity for a cell surface protein of an immune cell.

5. The bispecific antigen binding protein of claim 4, further comprising an immune checkpoint inhibitor.

6. A pharmaceutical composition comprising the antigen binding protein of claim 1 and a pharmaceutically acceptable carrier.

7. An antigen binding protein that specifically recognizes a target Melanoma-Associated Antigen A4 (MAGE-A4) peptide-MHC (pMHC), comprising:

(a) an antibody heavy chain variable (VH) domain comprising an HCDR1 amino acid sequence of SNYAMS (SEQ ID NO: 469), an HCDR2 amino acid sequence of IVSSGGTTYASWAKG (SEQ ID NO: 886), and an HCDR3 amino acid sequence of DLYYGPTTYSANL (SEQ ID NO: 727); and

(b) an antibody light chain variable (VL) domain comprising an LCDR1 amino acid sequence of TADTLRSYAS (SEQ ID NO: 472), an LCDR2 amino acid sequence of RDTSRPS (SEQ ID NO: 473), and an LCDR3 amino acid sequence of ATRDFSGSNFQL (SEQ ID NO: 875).

8. An antigen binding protein that specifically recognizes a target Melanoma-Associated Antigen A4 (MAGE-A4) peptide-MHC (pMHC), comprising:

(a) an antibody heavy chain variable (VH) domain comprising an HCDR1 amino acid sequence of SNYAMS (SEQ ID NO: 469), an HCDR2 amino acid sequence of IVSSGGTTYADSVKG (SEQ ID NO: 658), and an HCDR3 amino acid sequence of DLYYGPNTDYSAANL (SEQ ID NO: 732); and

(b) an antibody light chain variable (VL) domain comprising an LCDR1 amino acid sequence of TADTLRSYAS (SEQ ID NO: 472), an LCDR2 amino acid sequence of RDTSRPS (SEQ ID NO: 473), and an LCDR3 amino acid sequence of ATRPSSGSNFQA (SEQ ID NO: 880).

9. An antigen binding protein that specifically recognizes a target Melanoma-Associated Antigen A4 (MAGE-A4) peptide-MHC (pMHC), comprising:

- (a) an antibody heavy chain variable (VH) domain comprising an HCDR1 amino acid sequence of SNYAMS (SEQ ID NO: 469), an HCDR2 amino acid sequence of IVSSGGTTYASWAKG (SEQ ID NO: 624), and an HCDR3 amino acid sequence of DLYYGPTTYSANL (SEQ ID NO: 698); and
- (b) an antibody light chain variable (VL) domain comprising an LCDR1 amino acid sequence of TADTLRSYAS (SEQ ID NO: 472), an LCDR2 amino acid sequence of RDTSRPS (SEQ ID NO: 473), and an LCDR3 amino acid sequence of ATRPSSGSNFQA (SEQ ID NO: 846).

10. An antigen binding protein that specifically recognizes a target Melanoma-Associated Antigen A4 (MAGE-A4) peptide-MHC (pMHC), comprising:

- (a) an antibody heavy chain variable (VH) domain comprising an HCDR1 amino acid sequence of SNYAMS (SEQ ID NO: 469), an HCDR2 amino acid sequence of IVSSGGTTYASWAKG (SEQ ID NO: 470), and an HCDR3 amino acid sequence of DLYYGPTTYSANL (SEQ ID NO: 471); and
- (b) an antibody light chain variable (VL) domain comprising an LCDR1 amino acid sequence of TADTLRSYAS (SEQ ID NO: 472), an LCDR2 amino acid sequence of RDTSRPS (SEQ ID NO: 473), and an LCDR3 amino acid sequence of ATSDGSGSNFQL (SEQ ID NO: 474).

11. The antigen binding protein of claim 1, comprising:

- (a) an antibody heavy chain variable (VH) domain comprising a framework region, an HCDR1 region, an HCDR2 region, and an HCDR3 region, wherein the VH domain comprises an amino acid sequence set forth in SEQ ID NO: 583, or an amino acid sequence with at least 80% identity to the framework region of the amino acid sequence set forth in SEQ ID NO: 583 and 100% identity to the HCDR1 region, HCDR2 region, and HCDR3 region set forth in SEQ ID NO: 583; and
- (b) an antibody light chain variable (VL) domain comprising a framework region, an LCDR1 region, an LCDR2 region, and an LCDR3 region, wherein the VL domain comprises an amino acid sequence set forth in SEQ ID NO: 805, or an amino acid sequence with at least 80% identity to the framework region of the amino acid sequence set forth in

SEQ ID NO: 805 and 100% identity to the LCDR1 region, LCDR2 region, and LCDR3 region set forth in SEQ ID NO: 805.

12. The antigen binding protein of claim 7, comprising:

(a) an antibody heavy chain variable (VH) domain comprising a framework region, an HCDR1 region, an HCDR2 region, and an HCDR3 region, wherein the VH domain comprises an amino acid sequence set forth in SEQ ID NO: 579, or an amino acid sequence with at least 80% identity to the framework region of the amino acid sequence set forth in SEQ ID NO: 579 and 100% identity to the HCDR1 region, HCDR2 region, and HCDR3 region set forth in SEQ ID NO: 579; and

(b) an antibody light chain variable (VL) domain comprising a framework region, an LCDR1 region, an LCDR2 region, and an LCDR3 region, wherein the VL domain comprises an amino acid sequence set forth in SEQ ID NO: 801 or an amino acid sequence with at least 80% identity to the framework region of the amino acid sequence set forth in SEQ ID NO: 801 and 100% identity to the LCDR1 region, LCDR2 region, and LCDR3 region set forth in SEQ ID NO: 801.

13. The antigen binding protein of claim 8, comprising:

(a) an antibody heavy chain variable (VH) domain comprising a framework region, an HCDR1 region, an HCDR2 region, and an HCDR3 region, wherein the VH domain comprises an amino acid sequence set forth in SEQ ID NO: 584, or an amino acid sequence with at least 80% identity to the framework region of the amino acid sequence set forth in SEQ ID NO: 584 and 100% identity to the HCDR1 region, HCDR2 region, and HCDR3 region set forth in SEQ ID NO: 584; and

(b) an antibody light chain variable (VL) domain comprising a framework region, an LCDR1 region, an LCDR2 region, and an LCDR3 region, wherein the VL domain comprises an amino acid sequence set forth in SEQ ID NO: 806 or an amino acid sequence with at least 80% identity to the framework region of the amino acid sequence set forth in SEQ ID NO: 806 and 100% identity to the LCDR1 region, LCDR2 region, and LCDR3 region set forth in SEQ ID NO: 806.

14. The antigen binding protein of claim 9, comprising:

- (a) an antibody heavy chain variable (VH) domain comprising a framework region, an HCDR1 region, an HCDR2 region, and an HCDR3 region, wherein the VH domain comprises an amino acid sequence set forth in SEQ ID NO: 550, or an amino acid sequence with at least 80% identity to the framework region of the amino acid sequence set forth in SEQ ID NO: 550 and 100% identity to the HCDR1 region, HCDR2 region, and HCDR3 region set forth in SEQ ID NO: 550; and
- (b) an antibody light chain variable (VL) domain comprising a framework region, an LCDR1 region, an LCDR2 region, and an LCDR3 region, wherein the VL domain comprises an amino acid sequence set forth in SEQ ID NO: 772 or an amino acid sequence with at least 80% identity to the framework region of the amino acid sequence set forth in SEQ ID NO: 772 and 100% identity to the LCDR1 region, LCDR2 region, and LCDR3 region set forth in SEQ ID NO: 772.

15. The antigen binding protein of claim 1, comprising a single chain variable fragment (scFv), a Fab fragment, a Fab' fragment, a Fv fragment, or a diabody.

16. The bispecific antigen binding protein of claim 4, wherein the immune cell is selected from the group consisting of a T cell, a B cell, a natural killer (NK) cell, a natural killer T (NKT) cell, a neutrophil cell, a monocyte, and a macrophage.

17. The bispecific antigen binding protein of claim 4, wherein the cell surface protein of an immune cell is selected from the group consisting of CD3, TCR α , TCR β , CD16, NKG2D, CD89, CD64, and CD32.

18. The bispecific antigen binding protein of claim 4, wherein the at least first antigen binding domain comprises an scFv, and the at least second antigen binding domain comprises a Fab.

19. The bispecific antigen binding protein of claim 4, wherein the bispecific antigen binding protein is multivalent.

20. The bispecific antigen binding protein of claim 5, wherein the immune checkpoint inhibitor is selected from the group consisting of an anti-CTLA-4 antibody, an anti-PD-L1 antibody, an anti-PD-1 antibody, an anti-TIM-3 antibody, an anti-LAG-3 antibody, an anti-BTLA antibody, an anti-VISTA antibody, and combinations thereof.
21. The antigen binding protein of claim 8, wherein the antigen binding protein is a humanized antigen binding protein.
22. The antigen binding protein of claim 8, comprising a single chain variable fragment (scFv), a Fab fragment, a Fab' fragment, a Fv fragment, or a diabody.
23. A pharmaceutical composition comprising the antigen binding protein of claim 8, and a pharmaceutically acceptable carrier.
24. A bispecific antigen binding protein, comprising at least a first antigen binding domain comprising the antigen binding protein of claim 8, and at least a second antigen binding domain with specificity for a cell surface protein of an immune cell.
25. The bispecific antigen binding protein of claim 24, wherein the immune cell is selected from the group consisting of a T cell, a B cell, a natural killer (NK) cell, a natural killer T (NKT) cell, a neutrophil cell, a monocyte, and a macrophage.
26. The bispecific antigen binding protein of claim 24, wherein the cell surface protein of an immune cell is selected from the group consisting of CD3, TCR α , TCR β , CD16, NKG2D, CD89, CD64, and CD32.
27. The bispecific antigen binding protein of claim 24, wherein the at least first antigen binding domain comprises an scFv, and the at least second antigen binding domain comprises a Fab.
28. The bispecific antigen binding protein of claim 24, wherein the bispecific antigen binding protein is multivalent.

29. The bispecific antigen binding protein of claim 24, further comprising an immune checkpoint inhibitor.

30. The bispecific antigen binding protein of claim 29, wherein the immune checkpoint inhibitor is selected from the group consisting of an anti-CTLA-4 antibody, an anti-PD-L1 antibody, an anti-PD-1 antibody, an anti-TIM-3 antibody, an anti-LAG-3 antibody, an anti-BTLA antibody, an anti-VISTA antibody, and combinations thereof.