

ANTIBODIES TARGETING A COMPLEX COMPRISING NON-CLASSICAL HLA-I AND NEOANTIGEN AND THEIR METHODS OF USE

RELATED APPLICATIONS

[0001] The present application claims priority to U.S. Patent Application No. 17/199,205, filed March 11, 2021, now pending, and U.S. Provisional Patent Application No. 63/032,747, filed June 1, 2020; now pending, the entire contents of each of which are hereby incorporated by reference for all purposes.

SUMMARY

[0002] Disclosed herein, in certain embodiments, are monoclonal antibodies or antigen-binding fragments thereof, comprising a light chain variable domain (VL) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 7. Disclosed herein, in certain embodiments, are monoclonal antibodies or antigen-binding fragments thereof, comprising a light chain variable domain (VL) comprising an amino acid sequence at least 90% identical to an amino acid sequence set forth as SEQ ID NO: 7. Disclosed herein, in certain embodiments, are monoclonal antibodies or antigen-binding fragments thereof, comprising a light chain variable domain (VL) comprising an amino acid sequence at least 95% identical to an amino acid sequence set forth as SEQ ID NO: 7. Disclosed herein, in certain embodiments, are monoclonal antibodies or antigen-binding fragments thereof, comprising a light chain variable domain (VL) comprising an amino acid sequence at least 99% identical to an amino acid sequence set forth as SEQ ID NO: 7. Disclosed herein, in certain embodiments, are monoclonal antibodies or antigen-binding fragments thereof, comprising a light chain variable domain (VL) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 7. In some embodiments, the monoclonal antibody or antigen-binding fragment thereof comprises a heavy chain variable domain (VH) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 8. In some embodiments, the monoclonal antibody or antigen-binding fragment thereof comprises a heavy chain variable domain (VH) comprising an amino acid sequence at least 90% identical to an amino acid sequence set forth as SEQ ID NO: 8. In some embodiments, the monoclonal antibody or antigen-binding fragment thereof comprises a heavy chain variable domain (VH) comprising an amino acid sequence at least 95% identical to an amino acid

sequence set forth as SEQ ID NO: 8. In some embodiments, the monoclonal antibody or antigen-binding fragment thereof comprises a heavy chain variable domain (VH) comprising an amino acid sequence at least 99% identical to an amino acid sequence set forth as SEQ ID NO: 8. In some embodiments, the monoclonal antibody or antigen-binding fragment thereof comprises a heavy chain variable domain (VH) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 8. In some embodiments, the monoclonal antibody or antigen-binding fragment thereof selectively binds to a complex comprising an HLA-E and a neoantigen. In some embodiments, the monoclonal antibody or antigen-binding fragment thereof does not have a binding affinity to (i) the HLA-E alone; or (ii) the neoantigen alone. In some embodiments, the neoantigen is expressed by an antigen processing machinery (APM)-proficient cell. In some embodiments, the neoantigen is expressed by a TAP1/2-proficient cell. In some embodiments, the neoantigen comprises, consists essentially of, or consists of a sequence according to SEQ ID NO: 17 (VMAPRTLIL), SEQ ID NO: 18 (VMAPRTLFL), SEQ ID NO: 19 (VMAPRTLVL), SEQ ID NO: 20 (VTAPRTLLL), SEQ ID NO: 21 (IMAPRTLVL), SEQ ID NO: 23 (VMAPQALLL), SEQ ID NO: 24 (VMAPRALLL), SEQ ID NO: 25 (VMAPRTLALL), SEQ ID NO: 26 (VMAPRTLTL), SEQ ID NO: 27 (VMAPRTVLL), SEQ ID NO: 28 (VMPPTLLL), or SEQ ID NO: 29 (VTAPRTVLL). In some embodiments, the neoantigen comprises, consists essentially of, or consists of a sequence according to SEQ ID NO: 17 (VMAPRTLIL), SEQ ID NO: 18 (VMAPRTLFL), SEQ ID NO: 19 (VMAPRTLVL), SEQ ID NO: 26 (VMAPRTLTL), or SEQ ID NO: 27 (VMAPRTVLL). In some embodiments, the HLA-E is HLA-E*0101 or HLA-E*0103. In some embodiments, the antibody selectively binds to the complex comprising: (a) the HLA-E*0101 and the neoantigen; (b) the HLA-E*0103 and the neoantigen; or (c) the HLA-E*0101 and the neoantigen, and the HLA-E*0103 and the neoantigen. In some embodiments, the monoclonal antibody or antigen-binding fragment thereof is a murine antibody, a chimeric antibody, a camelid antibody, a humanized antibody, or a human antibody. In some embodiments, the monoclonal antibody or antigen-binding fragment thereof is a TCR-like antibody. In some embodiments, the monoclonal antibody or antigen-binding fragment thereof is a multispecific antibody. In some embodiments, the monoclonal antibody or antigen-binding fragment thereof is a bispecific antibody. In some embodiments, the monoclonal antibody or antigen-binding fragment thereof is a bispecific T cell engager (BiTE). In some embodiments, the BiTE binds to a CD3 protein associated with a T cell receptor (TCR). In some embodiments, the BiTE further comprises a light chain variable domain (VL) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 15. In some embodiments,

the BiTE further comprises a heavy chain variable domain (VH) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 16. In some embodiments, the monoclonal antibody or antigen-binding fragment thereof is a multifunctional antibody. In some embodiments, the monoclonal antibody or antigen-binding fragment thereof antibody further comprises a conjugated therapeutic moiety. In some embodiments, the selective binding of the antibody to the complex comprising the HLA-E and the neoantigen induces an immune response in a cell. In some embodiments, the immune response comprises activation of T cells. In some embodiments, the T cell is a CD8+ T cell. In some embodiments, the immune response comprises activation of cytotoxic T cells (CTLs). In some embodiments, the cell is a cancer cell.

[0003] Disclosed herein, in certain embodiments, are monoclonal antibodies or antigen-binding fragments thereof, comprising a heavy chain variable domain (VH) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 8. Disclosed herein, in certain embodiments, are monoclonal antibodies or antigen-binding fragments thereof, comprising a heavy chain variable domain (VH) comprising an amino acid sequence at least 90% identical to an amino acid sequence set forth as SEQ ID NO: 8. Disclosed herein, in certain embodiments, are monoclonal antibodies or antigen-binding fragments thereof, comprising a heavy chain variable domain (VH) comprising an amino acid sequence at least 95% identical to an amino acid sequence set forth as SEQ ID NO: 8. Disclosed herein, in certain embodiments, are monoclonal antibodies or antigen-binding fragments thereof, comprising a heavy chain variable domain (VH) comprising an amino acid sequence at least 99% identical to an amino acid sequence set forth as SEQ ID NO: 8. Disclosed herein, in certain embodiments, are monoclonal antibodies or antigen-binding fragments thereof, comprising a heavy chain variable domain (VH) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 8. In some embodiments, the monoclonal antibody or antigen-binding fragment thereof comprises a light chain variable domain (VL) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 7. In some embodiments, the monoclonal antibody or antigen-binding fragment thereof comprises a light chain variable domain (VL) comprising an amino acid sequence at least 90% identical to an amino acid sequence set forth as SEQ ID NO: 7. In some embodiments, the monoclonal antibody or antigen-binding fragment thereof comprises a light chain variable domain (VL) comprising an amino acid sequence at least 95% identical to an amino acid sequence set forth as SEQ ID NO: 7. In some embodiments, the monoclonal antibody or antigen-binding fragment thereof comprises a light chain variable domain (VL) comprising an amino acid

sequence at least 99% identical to an amino acid sequence set forth as SEQ ID NO: 7. In some embodiments, the monoclonal antibody or antigen-binding fragment thereof comprises a light chain variable domain (VL) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 7. In some embodiments, the monoclonal antibody or antigen-binding fragment thereof selectively binds to a complex comprising an HLA-E and a neoantigen. In some embodiments, the monoclonal antibody or antigen-binding fragment thereof does not have a binding affinity to (i) the HLA-E alone; or (ii) the neoantigen alone. In some embodiments, the neoantigen is expressed by an antigen processing machinery (APM)-proficient cell. In some embodiments, the neoantigen is expressed by a TAP1/2-proficient cell. In some embodiments, the neoantigen comprises, consists essentially of, or consists of a sequence according to SEQ ID NO: 17 (VMAPRTLIL), SEQ ID NO: 18 (VMAPRTLFL), SEQ ID NO: 19 (VMAPRTLVL), SEQ ID NO: 20 (VTAPRTLLL), SEQ ID NO: 21 (IMAPRTLVL), SEQ ID NO: 23 (VMAPQALLL), SEQ ID NO: 24 (VMAPRALLL), SEQ ID NO: 25 (VMAPRTLLL), SEQ ID NO: 26 (VMAPRTLTL), SEQ ID NO: 27 (VMAPRTVLL), SEQ ID NO: 28 (VMPPTLLL), or SEQ ID NO: 29 (VTAPRTVLL). In some embodiments, the neoantigen comprises, consists essentially of, or consists of a sequence according to SEQ ID NO: 17 (VMAPRTLIL), SEQ ID NO: 18 (VMAPRTLFL), SEQ ID NO: 19 (VMAPRTLVL), SEQ ID NO: 26 (VMAPRTLTL), or SEQ ID NO: 27 (VMAPRTVLL). In some embodiments, the HLA-E is HLA-E*0101 or HLA-E*0103. In some embodiments, the antibody selectively binds to the complex comprising: (a) the HLA-E*0101 and the neoantigen; (b) the HLA-E*0103 and the neoantigen; or (c) the HLA-E*0101 and the neoantigen, and the HLA-E*0103 and the neoantigen. In some embodiments, the monoclonal antibody or antigen-binding fragment thereof is a murine antibody, a chimeric antibody, a camelid antibody, a humanized antibody, or a human antibody. In some embodiments, the monoclonal antibody or antigen-binding fragment thereof is a TCR-like antibody. In some embodiments, the monoclonal antibody or antigen-binding fragment thereof is a multispecific antibody. In some embodiments, the monoclonal antibody or antigen-binding fragment thereof is a bispecific antibody. In some embodiments, the monoclonal antibody or antigen-binding fragment thereof is a bispecific T cell engager (BiTE). In some embodiments, the BiTE binds to a CD3 protein associated with a T cell receptor (TCR). In some embodiments, the BiTE further comprises a light chain variable domain (VL) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 15. In some embodiments, the BiTE further comprises a heavy chain variable domain (VH) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 16. In some embodiments,

the monoclonal antibody or antigen-binding fragment thereof is a multifunctional antibody. In some embodiments, the monoclonal antibody or antigen-binding fragment thereof antibody further comprises a conjugated therapeutic moiety. In some embodiments, the selective binding of the antibody to the complex comprising the HLA-E and the neoantigen induces an immune response in a cell. In some embodiments, the immune response comprises activation of T cells. In some embodiments, the T cell is a CD8+ T cell. In some embodiments, the immune response comprises activation of cytotoxic T cells (CTLs). In some embodiments, the cell is a cancer cell.

[0004] Disclosed herein, in certain embodiments, are monoclonal antibodies or antigen-binding fragments thereof, comprising a light chain complementarity determining region (CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 1-3. Disclosed herein, in certain embodiments, are monoclonal antibodies or antigen-binding fragments thereof, comprising a light chain complementarity determining region (CDR) having an amino acid sequence at least 90% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 1-3. Disclosed herein, in certain embodiments, are monoclonal antibodies or antigen-binding fragments thereof, comprising a light chain complementarity determining region (CDR) having an amino acid sequence at least 95% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 1-3. Disclosed herein, in certain embodiments, are monoclonal antibodies or antigen-binding fragments thereof, comprising a light chain complementarity determining region (CDR) having an amino acid sequence at least 99% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 1-3. Disclosed herein, in certain embodiments, are monoclonal antibodies or antigen-binding fragments thereof, comprising a light chain complementarity determining region (CDR) having an amino acid sequence 100% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 1-3. In some embodiments, the monoclonal antibody or antigen-binding fragment thereof comprises a heavy chain complementarity determining region (CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6. In some embodiments, the monoclonal antibody or antigen-binding fragment thereof comprises a heavy chain complementarity determining region (CDR) having an amino acid sequence at least 90% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6. In some embodiments, the monoclonal antibody or antigen-binding fragment thereof comprises a heavy chain complementarity determining region (CDR) having an amino acid sequence at least 95% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6. In some embodiments, the monoclonal antibody or

antigen-binding fragment thereof comprises a heavy chain complementarity determining region (CDR) having an amino acid sequence at least 99% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6. In some embodiments, the monoclonal antibody or antigen-binding fragment thereof comprises a heavy chain complementarity determining region (CDR) having an amino acid sequence 100% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6. In some embodiments, the monoclonal antibody or antigen-binding fragment thereof comprises a light chain variable domain (VL) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 7. In some embodiments, the monoclonal antibody or antigen-binding fragment thereof comprises a heavy chain variable domain (VH) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 8. In some embodiments, the monoclonal antibody or antigen-binding fragment thereof selectively binds to a complex comprising an HLA-E and a neoantigen. In some embodiments, the monoclonal antibody or antigen-binding fragment thereof does not have a binding affinity to (i) the HLA-E alone; or (ii) the neoantigen alone. In some embodiments, the neoantigen is expressed by an antigen processing machinery (APM)-proficient cell. In some embodiments, the neoantigen is expressed by a TAP1/2-proficient cell. In some embodiments, the neoantigen comprises, consists essentially of, or consists of a sequence according to SEQ ID NO: 17 (VMAPRTLIL), SEQ ID NO: 18 (VMAPRTLFL), SEQ ID NO: 19 (VMAPRTLVL), SEQ ID NO: 20 (VTAPRTLLL), SEQ ID NO: 21 (IMAPRTLVL), SEQ ID NO: 23 (VMAQALLL), SEQ ID NO: 24 (VMAPRALLL), SEQ ID NO: 25 (VMAPRTLLL), SEQ ID NO: 26 (VMAPRTLTL), SEQ ID NO: 27 (VMAPRTVLL), SEQ ID NO: 28 (VMPPTLLL), or SEQ ID NO: 29 (VTAPRTVLL). In some embodiments, the neoantigen comprises, consists essentially of, or consists of a sequence according to SEQ ID NO: 17 (VMAPRTLIL), SEQ ID NO: 18 (VMAPRTLFL), SEQ ID NO: 19 (VMAPRTLVL), SEQ ID NO: 26 (VMAPRTLTL), or SEQ ID NO: 27 (VMAPRTVLL). In some embodiments, the HLA-E is HLA-E*0101 or HLA-E*0103. In some embodiments, the antibody selectively binds to the complex comprising: (a) the HLA-E*0101 and the neoantigen; (b) the HLA-E*0103 and the neoantigen; or (c) the HLA-E*0101 and the neoantigen, and the HLA-E*0103 and the neoantigen. In some embodiments, the monoclonal antibody or antigen-binding fragment thereof is a murine antibody, a chimeric antibody, a camelid antibody, a humanized antibody, or a human antibody. In some embodiments, the monoclonal antibody or antigen-binding fragment thereof is a TCR-like antibody. In some embodiments, the monoclonal antibody or antigen-binding fragment thereof is a multispecific antibody. In some embodiments, the monoclonal antibody or antigen-

binding fragment thereof is a bispecific antibody. In some embodiments, the monoclonal antibody or antigen-binding fragment thereof is a bispecific T cell engager (BiTE). In some embodiments, the BiTE binds to a CD3 protein associated with a T cell receptor (TCR). In some embodiments, the BiTE further comprises a light chain complementarity determining region (CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 9-11. In some embodiments, the BiTE further comprises a heavy chain complementarity determining region (CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 12-14. In some embodiments, the BiTE further comprises a light chain variable domain (VL) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 15. In some embodiments, the BiTE further comprises a heavy chain variable domain (VH) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 16. In some embodiments, the monoclonal antibody or antigen-binding fragment thereof is a multifunctional antibody. In some embodiments, the monoclonal antibody or antigen-binding fragment thereof antibody further comprises a conjugated therapeutic moiety. In some embodiments, the selective binding of the antibody to the complex comprising the HLA-E and the neoantigen induces an immune response in a cell. In some embodiments, the immune response comprises activation of T cells. In some embodiments, the T cell is a CD8+ T cell. In some embodiments, the immune response comprises activation of cytotoxic T cells (CTLs). In some embodiments, the cell is a cancer cell.

[0005] Disclosed herein, in certain embodiments, are monoclonal antibodies or antigen-binding fragments thereof, comprising a heavy chain complementarity determining region (CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6. Disclosed herein, in certain embodiments, are monoclonal antibodies or antigen-binding fragments thereof, comprising a heavy chain complementarity determining region (CDR) having an amino acid sequence at least 90% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6. Disclosed herein, in certain embodiments, are monoclonal antibodies or antigen-binding fragments thereof, comprising a heavy chain complementarity determining region (CDR) having an amino acid sequence at least 95% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6. Disclosed herein, in certain embodiments, are monoclonal antibodies or antigen-binding fragments thereof, comprising a heavy chain complementarity determining region (CDR) having an amino acid sequence at least 99% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6. Disclosed herein, in certain embodiments,

are monoclonal antibodies or antigen-binding fragments thereof, comprising a heavy chain complementarity determining region (CDR) having an amino acid sequence 100% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6. In some embodiments, the monoclonal antibody or antigen-binding fragment comprises a light chain complementarity determining region (CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 1-3. In some embodiments, the monoclonal antibody or antigen-binding fragment comprises a light chain complementarity determining region (CDR) having an amino acid sequence at least 90% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 1-3. In some embodiments, the monoclonal antibody or antigen-binding fragment comprises a light chain complementarity determining region (CDR) having an amino acid sequence at least 95% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 1-3. In some embodiments, the monoclonal antibody or antigen-binding fragment comprises a light chain complementarity determining region (CDR) having an amino acid sequence at least 99% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 1-3. In some embodiments, the monoclonal antibody or antigen-binding fragment comprises a light chain complementarity determining region (CDR) having an amino acid sequence 100% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 1-3. In some embodiments, the monoclonal antibody or antigen-binding fragment thereof comprises a heavy chain variable domain (VH) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 8. In some embodiments, the monoclonal antibody or antigen-binding fragment thereof comprises a light chain variable domain (VL) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 7. In some embodiments, the monoclonal antibody or antigen-binding fragment thereof selectively binds to a complex comprising an HLA-E and a neoantigen. In some embodiments, the monoclonal antibody or antigen-binding fragment thereof does not have a binding affinity to (i) the HLA-E alone; or (ii) the neoantigen alone. In some embodiments, the neoantigen is expressed by an antigen processing machinery (APM)-proficient cell. In some embodiments, the neoantigen is expressed by a TAP1/2-proficient cell. In some embodiments, the neoantigen comprises, consists essentially of, or consists of a sequence according to SEQ ID NO: 17 (VMAPRTLIL), SEQ ID NO: 18 (VMAPRTLFL), SEQ ID NO: 19 (VMAPRTLVL), SEQ ID NO: 20 (VTAPRTLILL), SEQ ID NO: 21 (IMAPRTLVL), SEQ ID NO: 23 (VMA PQALLL), SEQ ID NO: 24 (VMA PRALLL), SEQ ID NO: 25 (VMA PRTLILL), SEQ ID NO: 26 (VMA PRTLTL), SEQ ID NO: 27 (VMA PRTVLL), SEQ ID NO: 28

(VMPPTLL), or SEQ ID NO: 29 (VTAPRTVLL). In some embodiments, the neoantigen comprises, consists essentially of, or consists of a sequence according to SEQ ID NO: 17 (VMAPRTLIL), SEQ ID NO: 18 (VMAPRTLFL), SEQ ID NO: 19 (VMAPRTLVL), SEQ ID NO: 26 (VMAPRTLTL), or SEQ ID NO: 27 (VMAPRTVLL). In some embodiments, the HLA-E is HLA-E*0101 or HLA-E*0103. In some embodiments, the antibody selectively binds to the complex comprising: (a) the HLA-E*0101 and the neoantigen; (b) the HLA-E*0103 and the neoantigen; or (c) the HLA-E*0101 and the neoantigen, and the HLA-E*0103 and the neoantigen. In some embodiments, the monoclonal antibody or antigen-binding fragment thereof is a murine antibody, a chimeric antibody, a camelid antibody, a humanized antibody, or a human antibody. In some embodiments, the monoclonal antibody or antigen-binding fragment thereof is a TCR-like antibody. In some embodiments, the monoclonal antibody or antigen-binding fragment thereof is a multispecific antibody. In some embodiments, the monoclonal antibody or antigen-binding fragment thereof is a bispecific antibody. In some embodiments, the monoclonal antibody or antigen-binding fragment thereof is a bispecific T cell engager (BiTE). In some embodiments, the BiTE binds to a CD3 protein associated with a T cell receptor (TCR). In some embodiments, the BiTE further comprises a light chain complementarity determining region (CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 9-11. In some embodiments, the BiTE further comprises a heavy chain complementarity determining region (CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 12-14. In some embodiments, the BiTE further comprises a light chain variable domain (VL) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 15. In some embodiments, the BiTE further comprises a heavy chain variable domain (VH) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 16. In some embodiments, the monoclonal antibody or antigen-binding fragment thereof is a multifunctional antibody. In some embodiments, the monoclonal antibody or antigen-binding fragment thereof further comprises a conjugated therapeutic moiety. In some embodiments, the selective binding of the antibody to the complex comprising the HLA-E and the neoantigen induces an immune response in a cell. In some embodiments, the immune response comprises activation of T cells. In some embodiments, the T cell is a CD8+ T cell. In some embodiments, the immune response comprises activation of cytotoxic T cells (CTLs). In some embodiments, the cell is a cancer cell.

[0006] Disclosed herein, in certain embodiments, are bispecific antibodies or antigen-binding fragments thereof, comprising: (a) a light chain complementarity determining region (CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 1-3; or a heavy chain complementarity determining region (CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6; and (b) a light chain complementarity determining region (CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 9-11; or a heavy chain complementarity determining region (CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 12-14. In some embodiments, the bispecific antibody comprises: (a) a light chain variable domain (VL) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 7; or a heavy chain variable domain (VH) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 8; and (b) a light chain variable domain (VL) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 15; or a heavy chain variable domain (VH) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 16. Disclosed herein, in certain embodiments, are bispecific antibodies or antigen-binding fragments thereof, comprising: (a) a light chain complementarity determining region (CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 1-3; and a heavy chain complementarity determining region (CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6; and (b) a light chain complementarity determining region (CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 9-11; and a heavy chain complementarity determining region (CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 12-14. In some embodiments, the bispecific antibody comprises: (a) a light chain variable domain (VL) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 7; and a heavy chain variable domain (VH) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 8; and (b) a light chain variable domain (VL) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 15; and a heavy chain variable domain (VH) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 16. In some embodiments,

the bispecific antibody selectively binds to a complex comprising an HLA-E and a neoantigen. In some embodiments, the bispecific antibody does not have a binding affinity to (i) the HLA-E alone; or (ii) the neoantigen alone. In some embodiments, the neoantigen is expressed by an antigen processing machinery (APM)-proficient cell. In some embodiments, the neoantigen is expressed by a TAP1/2-proficient cell. In some embodiments, the neoantigen comprises, consists essentially of, or consists of a sequence according to SEQ ID NO: 17 (VMAPRTLIL), SEQ ID NO: 18 (VMAPRTLFL), SEQ ID NO: 19 (VMAPRTLVL), SEQ ID NO: 20 (VTAPRTLIL), SEQ ID NO: 21 (IMAPRTLVL), SEQ ID NO: 23 (VMAQALLL), SEQ ID NO: 24 (VMAPRALLL), SEQ ID NO: 25 (VMAPRTLIL), SEQ ID NO: 26 (VMAPRTLTL), SEQ ID NO: 27 (VMAPRTVLL), SEQ ID NO: 28 (VMPRTLIL), or SEQ ID NO: 29 (VTAPRTVLL). In some embodiments, the neoantigen comprises, consists essentially of, or consists of a sequence according to SEQ ID NO: 17 (VMAPRTLIL), SEQ ID NO: 18 (VMAQALLL), SEQ ID NO: 19 (VMAQALVL), SEQ ID NO: 26 (VMAQRTLTL), or SEQ ID NO: 27 (VMAQRTVLL). In some embodiments, the HLA-E is HLA-E*0101 or HLA-E*0103. In some embodiments, the antibody selectively binds to the complex comprising: (a) the HLA-E*0101 and the neoantigen; (b) the HLA-E*0103 and the neoantigen; or (c) the HLA-E*0101 and the neoantigen, and the HLA-E*0103 and the neoantigen. In some embodiments, the monoclonal antibody or antigen-binding fragment thereof is a murine antibody, a chimeric antibody, a camelid antibody, a humanized antibody, or a human antibody. In some embodiments, the monoclonal antibody or antigen-binding fragment thereof is a bispecific T cell engager (BiTE). In some embodiments, the BiTE binds to a CD3 protein associated with a T cell receptor (TCR). In some embodiments, the monoclonal antibody or antigen-binding fragment thereof is a multifunctional antibody. In some embodiments, the monoclonal antibody or antigen-binding fragment thereof antibody further comprises a conjugated therapeutic moiety. In some embodiments, the selective binding of the antibody to the complex comprising the HLA-E and the neoantigen induces an immune response in a cell. In some embodiments, the immune response comprises activation of T cells. In some embodiments, the T cell is a CD8+ T cell. In some embodiments, the immune response comprises activation of cytotoxic T cells (CTLs). In some embodiments, the cell is a cancer cell.

[0007] Disclosed herein, in certain embodiments, are pharmaceutical compositions comprising: (a) a monoclonal antibody or an antigen-binding fragment thereof as disclosed herein, or a bispecific antibody or an antigen-binding fragment thereof as disclosed herein; and (b) a pharmaceutically acceptable carrier or excipient.

[0008] Disclosed herein, in certain embodiments, are methods of treating cancer in an individual in need thereof, comprising administering to the individual an effective amount of a monoclonal antibody or an antigen-binding fragment thereof comprising a light chain complementarity determining region (CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 1-3. Disclosed herein, in certain embodiments, are methods of treating cancer in an individual in need thereof, comprising administering to the individual an effective amount of a monoclonal antibody or an antigen-binding fragment thereof comprising a heavy chain complementarity determining region (CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6. In some embodiments, the monoclonal antibody or antigen-binding fragment thereof comprises (a) a light chain complementarity determining region (CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 1-3; and (b) a heavy chain complementarity determining region (CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6. In some embodiments, the monoclonal antibody or antigen-binding fragment thereof comprises (a) a light chain complementarity determining region (CDR) having an amino acid sequence at least 90% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 1-3; and (b) a heavy chain complementarity determining region (CDR) having an amino acid sequence at least 90% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6. In some embodiments, the monoclonal antibody or antigen-binding fragment thereof comprises (a) a light chain complementarity determining region (CDR) having an amino acid sequence at least 95% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 1-3; and (b) a heavy chain complementarity determining region (CDR) having an amino acid sequence at least 95% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6. In some embodiments, the monoclonal antibody or antigen-binding fragment thereof comprises (a) a light chain complementarity determining region (CDR) having an amino acid sequence at least 99% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 1-3; and (b) a heavy chain complementarity determining region (CDR) having an amino acid sequence at least 99% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6. In some embodiments, the monoclonal antibody or antigen-binding fragment thereof comprises (a) a light chain complementarity determining region (CDR) having an amino acid sequence 100% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 1-3; and (b) a heavy chain

complementarity determining region (CDR) having an amino acid sequence 100% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6. In some embodiments, the monoclonal antibody or antigen-binding fragment thereof comprises a light chain variable domain (VL) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 7. In some embodiments, the monoclonal antibody or antigen-binding fragment thereof comprises a heavy chain variable domain (VH) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 8. In some embodiments, the monoclonal antibody or antigen-binding fragment thereof selectively binds to a complex comprising an HLA-E and a neoantigen. In some embodiments, the monoclonal antibody or antigen-binding fragment thereof does not have a binding affinity to (i) the HLA-E alone; or (ii) the neoantigen alone. In some embodiments, the neoantigen is expressed by an antigen processing machinery (APM)-proficient cell. In some embodiments, the neoantigen is expressed by a TAP1/2-proficient cell. In some embodiments, the neoantigen comprises, consists essentially of, or consists of a sequence according to SEQ ID NO: 17 (VMAPRTLIL), SEQ ID NO: 18 (VMAPRTLFL), SEQ ID NO: 19 (VMAPRTLVL), SEQ ID NO: 20 (VTAPRTLILL), SEQ ID NO: 21 (IMAPRTLVL), SEQ ID NO: 23 (VMA PQALLL), SEQ ID NO: 24 (VMA PRALLL), SEQ ID NO: 25 (VMA PRTLILL), SEQ ID NO: 26 (VMA PRTLTL), SEQ ID NO: 27 (VMA PRTVLL), SEQ ID NO: 28 (VMPRTLILL), or SEQ ID NO: 29 (VTAPRTVLL). In some embodiments, the neoantigen comprises, consists essentially of, or consists of a sequence according to SEQ ID NO: 17 (VMAPRTLIL), SEQ ID NO: 18 (VMAPRTLFL), SEQ ID NO: 19 (VMAPRTLVL), SEQ ID NO: 26 (VMA PRTLTL), or SEQ ID NO: 27 (VMA PRTVLL). In some embodiments, the HLA-E is HLA-E*0101 or HLA-E*0103. In some embodiments, the antibody selectively binds to the complex comprising: (a) the HLA-E*0101 and the neoantigen; (b) the HLA-E*0103 and the neoantigen; or (c) the HLA-E*0101 and the neoantigen, and the HLA-E*0103 and the neoantigen. In some embodiments, the monoclonal antibody or antigen-binding fragment thereof is a murine antibody, a chimeric antibody, a camelid antibody, a humanized antibody, or a human antibody. In some embodiments, the monoclonal antibody or antigen-binding fragment thereof is a TCR-like antibody. In some embodiments, the monoclonal antibody or antigen-binding fragment thereof is a multispecific antibody. In some embodiments, the monoclonal antibody or antigen-binding fragment thereof is a bispecific antibody. In some embodiments, the monoclonal antibody or antigen-binding fragment thereof is a bispecific T cell engager (BiTE). In some embodiments, the BiTE binds to a CD3 protein associated with a T cell receptor (TCR). In some embodiments, the BiTE further

comprises a light chain complementarity determining region (CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 9-11. In some embodiments, the BiTE further comprises a heavy chain complementarity determining region (CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 12-14. In some embodiments, the BiTE further comprises a light chain variable domain (VL) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 15. In some embodiments, the BiTE further comprises a heavy chain variable domain (VH) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 16. In some embodiments, the monoclonal antibody or antigen-binding fragment thereof is a multifunctional antibody. In some embodiments, the monoclonal antibody or antigen-binding fragment thereof antibody further comprises a conjugated therapeutic moiety. In some embodiments, the selective binding of the antibody to the complex comprising the HLA-E and the neoantigen induces an immune response in a cell. In some embodiments, the immune response comprises activation of T cells. In some embodiments, the T cell is a CD8+ T cell. In some embodiments, the immune response comprises activation of cytotoxic T cells (CTLs). In some embodiments, the cancer is breast cancer. In some embodiments, the cancer is kidney cancer. In some embodiments, the cancer is lung cancer. In some embodiments, the cancer is ovarian cancer. In some embodiments, the cancer is colorectal cancer. In some embodiments, the cancer is pancreatic cancer. In some embodiments, the cancer is choriocarcinoma. In some embodiments, the cancer is non-small cell lung carcinoma (NSCLC). In some embodiments, the cancer is gastric cancer. In some embodiments, the cancer is cervical cancer. In some embodiments, the cancer is head and neck cancer. In some embodiments, the cancer is a myeloma. In some embodiments, the cancer is a leukemia. In some embodiments, the cancer is a lymphoma. In some embodiments, the cancer is acute myeloid leukemia (AML). In some embodiments, the cancer is multiple myeloma. In some embodiments, the cancer is a myelodysplastic syndrome. In some embodiments, the cancer is a B-cell malignancy. In some embodiments, the cancer is mantle cell lymphoma.

[0009] Disclosed herein, in certain embodiments, are methods of treating cancer in an individual in need thereof, comprising administering to the individual an effective amount of a bispecific antibody or an antigen-binding fragment thereof, comprising: (a) a light chain complementarity determining region (CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 1-3; or a heavy chain complementarity determining region

(CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6; and (b) a light chain complementarity determining region (CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 9-11; or a heavy chain complementarity determining region (CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 12-14. In some embodiments, the bispecific antibody comprises: (a) a light chain variable domain (VL) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 7; or a heavy chain variable domain (VH) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 8; and (b) a light chain variable domain (VL) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 15; or a heavy chain variable domain (VH) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 16. Disclosed herein, in certain embodiments, are methods of treating cancer in an individual in need thereof, comprising administering to the individual an effective amount of a bispecific antibody or an antigen-binding fragment thereof, comprising: (a) a light chain complementarity determining region (CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 1-3; and a heavy chain complementarity determining region (CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6; and (b) a light chain complementarity determining region (CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 9-11; and a heavy chain complementarity determining region (CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 12-14. In some embodiments, the bispecific antibody comprises: (a) a light chain variable domain (VL) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 7; and a heavy chain variable domain (VH) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 8; and (b) a light chain variable domain (VL) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 15; and a heavy chain variable domain (VH) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 16. In some embodiments, the bispecific antibody or antigen-binding fragment thereof selectively binds to a complex comprising an HLA-E and a neoantigen. In some embodiments, the bispecific antibody or antigen-binding fragment thereof

does not have a binding affinity to (i) the HLA-E alone; or (ii) the neoantigen alone. In some embodiments, the neoantigen is expressed by an antigen processing machinery (APM)-proficient cell. In some embodiments, the neoantigen is expressed by a TAP1/2-proficient cell. In some embodiments, the neoantigen comprises, consists essentially of, or consists of a sequence according to SEQ ID NO: 17 (VMAPRTLIL), SEQ ID NO: 18 (VMAPRTLFL), SEQ ID NO: 19 (VMAPRTLVL), SEQ ID NO: 20 (VTAPRTLLL), SEQ ID NO: 21 (IMAPRTLVL), SEQ ID NO: 23 (VMAPQALLL), SEQ ID NO: 24 (VMAPRALLL), SEQ ID NO: 25 (VMAPRTLLL), SEQ ID NO: 26 (VMAPRTLTL), SEQ ID NO: 27 (VMAPRTVLL), SEQ ID NO: 28 (VMPPTLLL), or SEQ ID NO: 29 (VTAPRTVLL). In some embodiments, the neoantigen comprises, consists essentially of, or consists of a sequence according to SEQ ID NO: 17 (VMAPRTLIL), SEQ ID NO: 18 (VMAPRTLFL), SEQ ID NO: 19 (VMAPRTLVL), SEQ ID NO: 26 (VMAPRTLTL), or SEQ ID NO: 27 (VMAPRTVLL). In some embodiments, the HLA-E is HLA-E*0101 or HLA-E*0103. In some embodiments, the bispecific antibody selectively binds to the complex comprising: (a) the HLA-E*0101 and the neoantigen; (b) the HLA-E*0103 and the neoantigen; or (c) the HLA-E*0101 and the neoantigen, and the HLA-E*0103 and the neoantigen. In some embodiments, the bispecific antibody or antigen-binding fragment thereof is a murine antibody, a chimeric antibody, a camelid antibody, a humanized antibody, or a human antibody. In some embodiments, the bispecific antibody or antigen-binding fragment thereof is a TCR-like antibody. In some embodiments, the bispecific antibody or antigen-binding fragment thereof is a bispecific T cell engager (BiTE). In some embodiments, the BiTE binds to a CD3 protein associated with a T cell receptor (TCR). In some embodiments, the bispecific antibody or antigen-binding fragment thereof is a multifunctional antibody. In some embodiments, the bispecific antibody or antigen-binding fragment thereof antibody further comprises a conjugated therapeutic moiety. In some embodiments, the selective binding of the antibody to the complex comprising the HLA-E and the neoantigen induces an immune response in a cell. In some embodiments, the immune response comprises activation of T cells. In some embodiments, the T cell is a CD8+ T cell. In some embodiments, the immune response comprises activation of cytotoxic T cells (CTLs). In some embodiments, the bispecific antibody is administered at a therapeutically effective amount. In some embodiments, the cancer is breast cancer. In some embodiments, the cancer is kidney cancer. In some embodiments, the cancer is lung cancer. In some embodiments, the cancer is ovarian cancer. In some embodiments, the cancer is colorectal cancer. In some embodiments, the cancer is pancreatic cancer. In some embodiments, the cancer is choriocarcinoma. In some embodiments, the cancer is non-small cell lung carcinoma

(NSCLC). In some embodiments, the cancer is gastric cancer. In some embodiments, the cancer is cervical cancer. In some embodiments, the cancer is head and neck cancer. In some embodiments, the cancer is a myeloma. In some embodiments, the cancer is a leukemia. In some embodiments, the cancer is a lymphoma. In some embodiments, the cancer is acute myeloid leukemia (AML). In some embodiments, the cancer is multiple myeloma. In some embodiments, the cancer is a myelodysplastic syndrome. In some embodiments, the cancer is a B-cell malignancy. In some embodiments, the cancer is mantle cell lymphoma.

[0010] Disclosed herein, in certain embodiments, are monoclonal antibodies or antigen-binding fragments thereof, comprising a light chain (LC) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 31. Disclosed herein, in certain embodiments, are monoclonal antibodies or antigen-binding fragments thereof, comprising a light chain (LC) comprising an amino acid sequence at least 90% identical to an amino acid sequence set forth as SEQ ID NO: 31. Disclosed herein, in certain embodiments, are monoclonal antibodies or antigen-binding fragments thereof, comprising a light chain (LC) comprising an amino acid sequence at least 95% identical to an amino acid sequence set forth as SEQ ID NO: 31. Disclosed herein, in certain embodiments, are monoclonal antibodies or antigen-binding fragments thereof, comprising a light chain (LC) comprising an amino acid sequence at least 99% identical to an amino acid sequence set forth as SEQ ID NO: 31. Disclosed herein, in certain embodiments, are monoclonal antibodies or antigen-binding fragments thereof, comprising a light chain (LC) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 31. In some embodiments, the monoclonal antibody or antigen-binding fragment thereof comprises a heavy chain (HC) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 30. In some embodiments, the monoclonal antibody or antigen-binding fragment thereof comprises a heavy chain (HC) comprising an amino acid sequence at least 90% identical to an amino acid sequence set forth as SEQ ID NO: 30. In some embodiments, the monoclonal antibody or antigen-binding fragment thereof comprises a heavy chain (HC) comprising an amino acid sequence at least 95% identical to an amino acid sequence set forth as SEQ ID NO: 30. In some embodiments, the monoclonal antibody or antigen-binding fragment thereof comprises a heavy chain (HC) comprising an amino acid sequence at least 99% identical to an amino acid sequence set forth as SEQ ID NO: 30. In some embodiments, the monoclonal antibody or antigen-binding fragment thereof comprises a heavy chain (HC) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 30. In some embodiments, the monoclonal antibody or antigen-binding fragment

thereof comprises a heavy chain (HC) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 32. In some embodiments, the monoclonal antibody or antigen-binding fragment thereof comprises a heavy chain (HC) comprising an amino acid sequence at least 90% identical to an amino acid sequence set forth as SEQ ID NO: 32. In some embodiments, the monoclonal antibody or antigen-binding fragment thereof comprises a heavy chain (HC) comprising an amino acid sequence at least 95% identical to an amino acid sequence set forth as SEQ ID NO: 32. In some embodiments, the monoclonal antibody or antigen-binding fragment thereof comprises a heavy chain (HC) comprising an amino acid sequence at least 99% identical to an amino acid sequence set forth as SEQ ID NO: 32. In some embodiments, the monoclonal antibody or antigen-binding fragment thereof comprises a heavy chain (HC) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 32. In some embodiments, the monoclonal antibody or antigen-binding fragment thereof comprises a heavy chain (HC) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 33. In some embodiments, the monoclonal antibody or antigen-binding fragment thereof comprises a heavy chain (HC) comprising an amino acid sequence at least 90% identical to an amino acid sequence set forth as SEQ ID NO: 33. In some embodiments, the monoclonal antibody or antigen-binding fragment thereof comprises a heavy chain (HC) comprising an amino acid sequence at least 95% identical to an amino acid sequence set forth as SEQ ID NO: 33. In some embodiments, the monoclonal antibody or antigen-binding fragment thereof comprises a heavy chain (HC) comprising an amino acid sequence at least 99% identical to an amino acid sequence set forth as SEQ ID NO: 33. In some embodiments, the monoclonal antibody or antigen-binding fragment thereof comprises a heavy chain (HC) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 33. Disclosed herein, in certain embodiments, are monoclonal antibodies or antigen-binding fragments thereof, comprising a light chain (LC) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 35. Disclosed herein, in certain embodiments, are monoclonal antibodies or antigen-binding fragments thereof, comprising a light chain (LC) comprising an amino acid sequence at least 90% identical to an amino acid sequence set forth as SEQ ID NO: 35. Disclosed herein, in certain embodiments, are monoclonal antibodies or antigen-binding fragments thereof, comprising a light chain (LC) comprising an amino acid sequence at least 95% identical to an amino acid sequence set forth as SEQ ID NO: 35. Disclosed herein, in certain embodiments, are monoclonal antibodies or antigen-binding fragments thereof, comprising a light chain (LC) comprising an amino acid sequence at least 99% identical to an amino acid sequence

set forth as SEQ ID NO: 35. Disclosed herein, in certain embodiments, are monoclonal antibodies or antigen-binding fragments thereof, comprising a light chain (LC) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 35. In some embodiments, the monoclonal antibody or antigen-binding fragment thereof comprises a heavy chain (HC) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 34. In some embodiments, the monoclonal antibody or antigen-binding fragment thereof comprises a heavy chain (HC) comprising an amino acid sequence at least 90% identical to an amino acid sequence set forth as SEQ ID NO: 34. In some embodiments, the monoclonal antibody or antigen-binding fragment thereof comprises a heavy chain (HC) comprising an amino acid sequence at least 95% identical to an amino acid sequence set forth as SEQ ID NO: 34. In some embodiments, the monoclonal antibody or antigen-binding fragment thereof comprises a heavy chain (HC) comprising an amino acid sequence at least 99% identical to an amino acid sequence set forth as SEQ ID NO: 34. In some embodiments, the monoclonal antibody or antigen-binding fragment thereof comprises a heavy chain (HC) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 34. In some embodiments, the monoclonal antibody or antigen-binding fragment thereof selectively binds to a complex comprising an HLA-E and a neoantigen. In some embodiments, the monoclonal antibody or antigen-binding fragment thereof does not have a binding affinity to (i) the HLA-E alone; or (ii) the neoantigen alone. In some embodiments, the neoantigen is expressed by an antigen processing machinery (APM)-proficient cell. In some embodiments, the neoantigen is expressed by a TAP1/2-proficient cell. In some embodiments, the neoantigen comprises, consists essentially of, or consists of a sequence according to SEQ ID NO: 17 (VMAPRTLIL), SEQ ID NO: 18 (VMAPRTLFL), SEQ ID NO: 19 (VMAPRTLVL), SEQ ID NO: 20 (VTAPRTLLL), SEQ ID NO: 21 (IMAPRTLVL), SEQ ID NO: 23 (VMAPQALLL), SEQ ID NO: 24 (VMAPRALLL), SEQ ID NO: 25 (VMAPRTLLL), SEQ ID NO: 26 (VMAPRTLTL), SEQ ID NO: 27 (VMAPRTVLL), SEQ ID NO: 28 (VMPPTLLL), or SEQ ID NO: 29 (VTAPRTVLL). In some embodiments, the neoantigen comprises, consists essentially of, or consists of a sequence according to SEQ ID NO: 17 (VMAPRTLIL), SEQ ID NO: 18 (VMAPRTLFL), SEQ ID NO: 19 (VMAPRTLVL), SEQ ID NO: 26 (VMAPRTLTL), or SEQ ID NO: 27 (VMAPRTVLL). In some embodiments, the HLA-E is HLA-E*0101 or HLA-E*0103. In some embodiments, the antibody selectively binds to the complex comprising: (a) the HLA-E*0101 and the neoantigen; (b) the HLA-E*0103 and the neoantigen; or (c) the HLA-E*0101 and the neoantigen, and the HLA-E*0103 and the neoantigen. In some embodiments, the monoclonal antibody or antigen-binding fragment thereof

is a murine antibody, a chimeric antibody, a camelid antibody, a humanized antibody, or a human antibody. In some embodiments, the monoclonal antibody or antigen-binding fragment thereof is a TCR-like antibody. In some embodiments, the monoclonal antibody or antigen-binding fragment thereof is a multispecific antibody. In some embodiments, the monoclonal antibody or antigen-binding fragment thereof is a bispecific antibody. In some embodiments, the monoclonal antibody or antigen-binding fragment thereof is a bispecific T cell engager (BiTE). In some embodiments, the BiTE binds to a CD3 protein associated with a T cell receptor (TCR). In some embodiments, the BiTE further comprises a light chain (LC) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 15. In some embodiments, the BiTE further comprises a heavy chain (HC) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 16. In some embodiments, the monoclonal antibody or antigen-binding fragment thereof is a multifunctional antibody. In some embodiments, the monoclonal antibody or antigen-binding fragment thereof antibody further comprises a conjugated therapeutic moiety. In some embodiments, the selective binding of the antibody to the complex comprising the HLA-E and the neoantigen induces an immune response in a cell. In some embodiments, the immune response comprises activation of T cells. In some embodiments, the T cell is a CD8+ T cell. In some embodiments, the immune response comprises activation of cytotoxic T cells (CTLs). In some embodiments, the cell is a cancer cell.

BRIEF DESCRIPTION OF THE DRAWINGS

[0011] The novel features of the invention are set forth with particularity in the appended claims. A better understanding of the features and advantages of the present invention will be obtained by reference to the following detailed description that sets forth illustrative embodiments, in which the principles of the invention are utilized, and the accompanying drawings of which:

[0012] **Fig. 1A-Fig. 1D** exemplifies identification and affinity characterization of CDRH3 region of R4 clone 1 (R4c1) against V-0025 and V-0018 (control). Phage (**Fig. 1A**) and monoclonal soluble ELISA(**Fig. 1B**). Antigen is at 1 µg/ml. Binding affinity sensorgram (**Fig. 1C**) and kinetic data (**Fig. 1D**).

[0013] **Fig. 2A-Fig. 2D** are exemplary overview of sorting schematic for the isolation of affinity matured R4c1. **Fig. 2A-Fig. 2C** exemplify cell sorting plots showing each round of sorting for the first round of affinity maturation. The 'star' indicates the sorted population. For the R4 sort (**Fig.**

2D), Koff was utilized with V-0025 at 10nM using R4c1-IgG1 at 1 μ M for the various timepoints as the antibody sink.

[0014] **Fig. 3A-Fig. 3G** exemplify clones identified from affinity maturation of R4c1. **Fig. 3A-Fig. 3D** exemplify binding profile to target antigen (V-0025) at 100nM. **Fig. 3E-Fig. 3G** exemplify binding profile of the clone, R2A_1, to target (V-0025) at 10nM and to additional peptide/HLA-E antigens at 100nM.

[0015] **Fig. 4** exemplifies R2A_1 binding to A549-B4 cells.

[0016] **Fig. 5A-Fig. 5B** exemplify isolation process for improved clones by affinity maturation of CDRL3 region of R2A_1. **Fig. 5A** exemplifies binding to target (V-0025) by parent clone (R2A_1) and the starting affinity maturation library (R0) and first round sorted library (R1). **Fig. 5B** exemplifies Koff of R1 affinity maturation library. Target (V-0025) is at 10nM, with R2A_1-hIgG1 as antibody sink at 1 μ M for 15 minutes up to 90 minutes.

[0017] **Fig. 6A-Fig. 6B** exemplify the sorting schematic for the isolation of clones with greater binding affinity than the parent. Cell sorting plots showing round 1 (**Fig. 6A**) and round 2 (**Fig. 6B**) sorting for affinity maturation. The asterisk indicates the sorted population. For the R2 sort, Koff was utilized with V-0025 at 10nM using R2A_1-IgG1 at 1 μ M for 45 minutes as the antibody sink.

[0018] **Fig. 7** exemplifies identification of clones from affinity maturation of the CDRL3 region of R2A_1 and binding profile to V-0025 at 1nM and 0.1nM. Arrows indicate the top clones.

[0019] **Fig. 8A-Fig. 8B** exemplify QC data for the production of ABX0020.

[0020] **Fig. 9A-Fig. 9I** exemplify affinity, specificity and stability of ABX0020. Specificity to peptide/HLA-E complexes by HLA-E clone 3D12 (**Fig. 9A**) and ABX0020 (**Fig. 9B**). Antibodies were used at 1 μ g/ml, antigen was used at 0.25 μ g/ml. **Fig. 9C** exemplifies monovalent affinity of ABX0020 to V-0025. **Fig. 9D** illustrates titration of V-0034. ABX0020 and HLA-E were used at 1 μ g/mL while V-0034 was titrated from 2 μ g/mL down to 122 pg/mL (1.22x10⁻⁴ μ g/mL). **Fig. 9E** illustrates titration of antibody. V-0034 used at 0.25 μ g/mL while ABX0020 and HLA-E were titrated from 2 μ g/mL down to 122 pg/mL (1.22x10⁻⁴ μ g/mL). **Fig. 9F** exemplifies thermostability of ABX0020. Binding affinity at 4°C compared with incubation at 37°C for 7 to 14 days using 1 μ g/ml of antibody and 0.25 μ g/ml of antigen. **Fig. 9G** illustrates binding of HLA-E to peptide-pulsed K562.E cells. K562.E cells were pulsed with 2 μ M of peptide for two hours followed by staining with antibody at 1 μ g/mL. **Fig. 9H** illustrates binding of ABX0020 to peptide-pulsed K562.E cells. K562.E cells were pulsed with 2 μ M of peptide for two hours followed by staining with antibody at 1 μ g/mL. **Fig. 9I** illustrates binding of ABX0020 to peptide-pulsed K562.E cells.

K562.E cells were pulsed with 2 μ M of peptide for two hours followed by staining with antibody at 1 μ g/mL.

[0021] **Fig. 10A-Fig. 10B** exemplify ABX0020 binds similarly to HLA-E*0101 and HLA-E*0103. **Fig. 10A** illustrates binding by HLA-E at 1 μ g/mL. **Fig. 10B** illustrates binding by ABX0020 at 1 μ g/mL.

[0022] **Fig. 11A-Fig. 11D** exemplify ABX0020 binds to a variety of tumor cell lines. Antibody binding at 1 μ g/mL. **Fig. 11A** exemplifies binding to IFN γ -stimulated JEG3 wild type cells (WT, top panel), JEG3 E^{KO} cells (middle panel) and JEG3 Tap-1^{KO} cells (bottom panel). **Fig. 11B** exemplifies binding to WT K-562 cells (top panel), HLA-E+ K-562 cells (middle panel) and HLA-E+ K-562 cells pulsed with 2 μ M of peptide. **Fig. 11A-Fig. 11B**, the light gray solid line represents isotype while the black outline represents HLA-E or ABX0020. **Fig. 11C** exemplifies binding in unstimulated (dotted black line) and IFN γ -stimulated (solid black line) THP-1 cells (top panel), RPMI-8226 cells (middle panel) and JY-A2 cells (bottom panel). **Fig. 11D** exemplifies binding to IFN γ -stimulated (solid black line) COLO-205 cells (top panel), PANC-1 cells (second from top panel), A549-D5 cells (second from bottom panel) and JVM2 cells (bottom panel). **Fig. 11C-Fig. 11D**, the gray solid line represents isotype and the dotted line represents unstimulated cells.

[0023] **Fig. 12A-Fig. 12I** exemplify ABX0020 enhances NK cytotoxicity against tumor cell lines expressing target. (**Fig. 12A-Fig. 12B**). **Fig. 12A** exemplifies frequency of dead target cells. NK cells were co-cultured for four hrs with IFN γ -stimulated and peptide-pulsed JY-A2 cells with MabCtrl (isotype control), ABX0020, ABX0021 or ABX0022. **Fig. 12B** exemplifies frequency of CD107a+ NK cells. N = 6. NK cells were co-cultured for four hrs with IFN γ -stimulated and peptide-pulsed JY-A2 cells with MabCtrl (isotype control), ABX0020, ABX0021 or ABX0022. (**Fig. 12C-Fig. 12D**) **Fig. 12C** illustrates NK cells co-cultured for 24 hrs with unstimulated and peptide-pulsed JY-A2 cells with MabCtrl, α NKG2A or ABX002. **Fig. 12D** illustrates NK cells co-cultured for 24 hrs with IFN γ -stimulated and peptide-pulsed JY-A2 cells with MabCtrl, α NKG2A or ABX0021. Both figures 12C and 12D show percent cytotoxicity as measured by LDH release with target only set to 0. N = 6. **Fig. 12E** illustrates NK cells co-cultured with peptide-pulsed HLA-E+ K-562 cells (K562.E) for four hrs with hIgG (isotype control) α NKG2A or ABX0021. The percent of dead K562.E is shown. N = 8. **Fig. 12F** illustrates NK cells co-cultured with unstimulated RPMI 8226 for 24 hrs with MabCtrl, ABX0020, ABX0021 or ABX0022. The frequency of dead RPMI 8226 is shown. N = 4. **Fig. 12G** illustrates NK cells co-cultured with IFN γ -stimulated and peptide-pulsed JY-A2 cells for four hrs with hIgG1, α NKG2A, or a titration of ABX0020 or ABX0022.

Fig. 12G shows frequency of dead target cells. **Fig. 12H** illustrates NK cells co-cultured with IFN γ -stimulated and peptide-pulsed JY-A2 cells for four hrs with hIgG1, α NKG2A, or a titration of ABX0020 or ABX0022. **Fig. 12H** shows frequency of CD107a+ NK cells. N = 6. **Fig. 12I** illustrates NK cells co-cultured with IFN γ -stimulated COLO-205 cells for four hrs with hIgG1 (control), cetuximab, ABX0020, ABX0021 or a combination of cetuximab with ABX0020 or ABX0021. The frequency of dead COLO-205 cells is shown. N = 11. MabCtrl, hIgG1, ABX0020, ABX0021 and α NKG2A were used at 10 μ g/mL unless otherwise indicated. ABX0022 was used at 1 μ g/mL unless otherwise indicated. Cetuximab was used at 0.1 μ g/mL. The effector to target ratio (E:T) was set to 10:1. Plots are shown as box and whiskers with means indicated by crosses. The whiskers are drawn down to the 25th percentile minus 1.5 times IQR (inter-quartile distance; the difference between the 25th and 75th percentiles). Outliers are plotted individually. *p<0.05; **p<0.01; ***p<0.001.

[0024] **Fig. 13** exemplifies that ABX0020 unleashes suppression of antigen-specific CD8+ T-cells and promotes lysis of target cells. Two different donor flu antigen (M1)-specific CTL lines were used in the study. (Donor A) CTL line provided by Professor van Hall at Leiden University Medical Center in the Netherlands and (Donor B) CTL line purchased from Astarte Biologics, WA, USA).

[0025] **Fig. 14A-Fig. 14B** illustrate design and characterization of ABX0040 Bispecific T-cell engager.

[0026] **Fig. 15** exemplifies affinity analysis of ABX0040.

[0027] **Fig. 16A-Fig. 16B** exemplify that ABX0040 staining to tumor cell line is HLA-E restricted. ABX0040 stains the JEG3 wild-type cells while not staining JEG3 cells lacking HLA-E. ABX0023 (ABX0020 derived with mouse-IgG) was used as a control.

[0028] **Fig. 17** exemplifies that ABX0040 stains target positive THP-1 AML cells. THP-1 cells were incubated O/N in the presence of human IFN-g (10ng/ml) and then stained with ABX0040 at 1 μ g/ml. Bound ABX0040 was detected using a goat anti-human IgG (GAH)-APC conjugate.

[0029] **Fig. 18A-Fig. 18E** are exemplary histograms to illustrate that ABX0040 stains human CD3+ cells and not CD3neg cells. **Fig. 18A** illustrates PBMCs stained with GAH-APC conjugate and anti-CD3 (clone SK7). **Fig. 18B** illustrates PBMCs stained with anti-CD4 and GAH-APC conjugate.

Fig. 18C illustrates CD3+ cell staining with ABX0040 + GAH-APC conjugate (no SK7 Ab). **Fig. 18D** illustrates double staining with anti-CD4-PE and ABX0040 + GAH-APC conjugate. Notice in this panel the two populations of CD3+ cells representing CD4+ and CD8+ T-cells. **Fig. 18E** illustrates double staining of CD3+ cells using ABX0040 and clone SK7-PE. ABX0040 was used at 1 μ g/mL.

[0030] **Fig. 19A-Fig. 19C** exemplify that ABX0040 mediates CD8+ T-cell lysis of target positive K562.E cells. Percent cytotoxicity was measured by the frequency of dead target cells with target only set to 0. Cells were harvested after 48 hrs using an effector to target ratio (E:T) of 5:1. (**Fig. 19A**) **Fig. 19B-19C** shows ABX0040 dose-dependent effect on CD8+ T cell activation, specifically CD107a (**Fig. 19B**) and IFN γ expression (**Fig. 19C**).

[0031] **Fig. 20A-Fig. 20E** exemplify that ABX0040 mediates CD8+ T-cell killing of THP-1 AML cells. **Fig. 20A** shows a dose-dependent effect (1000 to 80 pM) of ABX0040 to redirect CD8+ T cell cytotoxicity of THP-1 cells. Percent cytotoxicity was measured by the frequency of dead THP-1 cells with target only set to 0. **Fig. 20A-20E** shows ABX0040 dose-dependent effect on CD8+ T cell activation, specifically CD25 (**Fig. 20B**), CD107a (**Fig. 20C**), perforin (**Fig. 20D**), and IFN γ (**Fig. 20E**) expression. Cells were harvested after 48 hrs using an effector to target ratio (E:T) of 5:1.

[0032] **Fig. 21A-Fig. 21B** exemplify ABX0040 displays checkpoint blocking activity to activate NK cells. NK cells were co-cultured with K562.E cells (**Fig. 21A**) or RPMI-8226 cells (**Fig. 21B**) for 24 hrs. Both figures show percent cytotoxicity as measured by LDH release with target only set to 0. Antibody were used at 10 μ g/mL.

[0033] **Fig. 22A-Fig.22B** exemplify ABX0023 binding to immune cells. While immune cells express HLA-E and classical HLA type I, only NK cells and monocytes exhibit binding by ABX0023. Total PBMCs, enriched or purified cells were tested for the expression of HLA-E, classical HLA type I (HLA-A,B,C), or ABX0023. Gray represents isotype staining and the black line represents antibody staining. Platelet staining is representative of 2 donors. B cell staining is representative of 6 donors. T cell and NK cell staining is representative of 10 donors. Neutrophil and eosinophil staining is representative of 7 donors. DC staining is representative of 4 donors. Monocyte staining is representative of 4 donors. Macrophage staining is representative of 10 donors. N/T means not tested.

[0034] **Fig. 23A-Fig.23B** exemplify that stimulation of PBMCs with IFN γ does not induce ABX0023 binding. PBMCs were stimulated overnight (**Fig.23B**) with or (**Fig.23A**) without IFN γ and tested for the expression of HLA-E (clone 3D12), denatured-HLA-E (clone MEM-E/02) or ABX0023. Gray represents isotype staining and black line represents antibody staining. Staining is representative of 2 donors.

[0035] **Fig. 24** exemplifies that HLA-E positive HLA-A class I positive cell lines exhibit ABX0023 binding without stimulation. Either ABX0023 (mouse Fc) or ABX0020 (human Fc) was used for

staining, depending on cell line Fc receptor expression. Gray represents isotype staining and black line represents antibody staining. N/T means not tested.

[0036] **Fig. 25** exemplifies that cell lines that exhibit ABX0023 binding without stimulation show an increase in ABX0023 binding with IFN γ stimulation. Cells were stimulated for 24 hrs with IFN γ . Either ABX0023 (mouse Fc) or ABX0020 (human Fc) was used for staining, depending on cell line Fc receptor expression. Gray represents isotype staining and black line represents antibody staining. N/T means not tested.

[0037] **Fig. 26A-Fig. 26B** exemplifies that some cell lines require stimulation with IFN γ for ABX0023 binding. Cells were (**Fig. 26A**) left in culture or (**Fig. 26B**) stimulated with IFN γ for 24 hrs prior to staining. Gray represents isotype staining and black line represents antibody staining. N/T means not tested.

[0038] **Fig. 27** exemplifies that cell lines without HLA-E do not exhibit ABX0023 binding. Either ABX0023 (mouse Fc) or ABX0020 (human Fc) was used for staining. Gray represents isotype staining and black line represents antibody staining.

[0039] **Fig. 28A-Fig. 28B** exemplify that HLA-E and Tap1 peptide processing is required for ABX0023 binding. (**Fig. 28A**) JEG3 cells were stimulated for 24 hrs with IFN γ for 24 hrs prior to staining. (**Fig. 28B**) OCI-AML3 cells were unstimulated. Either ABX0023 (mouse Fc) or ABX0020 (human Fc) was used for staining. Gray represents isotype staining and black line represents antibody staining. N/T means not tested.

[0040] **Fig. 29** exemplifies that ABX0023 stains K562.E cells pulsed with specific peptide. K562 and K562.HLA-E + V-0025 (VMAPRTLFL) peptide pulsed cells were pelleted, treated with OCI compound and flash frozen to prepare frozen cell blocks for immunohistochemistry. ABX0023 antibody (2.25ug/ml) was used to stain K562.E + V-0025 and K562 cells. The panel on the left shows positive ABX0023 staining while control cells (right panel) are not stained.

[0041] **Fig. 30** exemplifies positive ABX0023 staining of human placenta tissue and specifically trophoblast cells.

[0042] **Fig. 31A- Fig. 31B** exemplify frozen section samples of head and neck tumor and normal adjacent tissue (NAT). **Fig. 31A** shows (panel left) staining with anti-HLA-E antibody (2.25ug/ml) and (panel right) with ABX0023 antibody (2.25ug/ml). **Fig. 31B** shows (panel left) NAT staining with anti-HLA-E antibody but not with ABX0023 antibody (panel right).

[0043] **Fig. 32A-Fig. 32B** exemplify frozen section samples of colon adenocarcinoma and NAT. **Fig. 32A** shows (panel left) staining with anti-HLA-E antibody (2.25ug/ml) and (panel right) with

ABX0023 antibody (2.25ug/ml). **Fig. 32B** shows little to no ABX0023 staining of normal adjacent colon tissue.

[0044] **Fig. 33A-Fig. 33B** exemplify frozen section samples of lung squamous cell carcinoma and NAT. **Fig. 33A** shows (panel left) staining with anti-HLA-E antibody (2.25ug/ml) and (panel right) with ABX0023 antibody (2.25ug/ml). **Fig. 33B** does not show ABX0023 staining of normal adjacent lung tissue.

[0045] **Fig. 34** demonstrates ABX0023 binding selectivity to targets in a colon adenocarcinoma tissue sample.

DETAILED DESCRIPTION

[0046] Disclosed herein, in certain embodiments, are antibodies comprising at least one heavy chain comprising a heavy chain variable domain (VH) and at least one light chain comprising a light chain variable domain (VL). Each VH and VL comprises three complementarity determining regions (CDR). In some embodiments, the antibodies are bispecific antibodies. In some embodiments, the bispecific antibodies are bispecific T cell engagers (BiTEs). In some embodiments, the bispecific antibodies bind to a CD3 protein associated with a T cell receptor (TCR). Further disclosed herein, in certain embodiments, are methods of treating a cancer by administering an antibody that selectively binds to a complex comprising a non-classical HLA-I (e.g. HLA-E) and a neoantigen. In some embodiments, the antibodies that selectively bind to a complex comprising a non-classical HLA-I (e.g. HLA-E) and a neoantigen modulate immune response against cancer cells, thereby treating cancer. In some embodiments, the antibodies are bispecific antibodies.

[0047] Traditional approaches to the treatment of cancers have included surgery, radiation, chemotherapy and hormone therapy. However, such therapies have not proven effective by themselves. Development of alternate remedies for preventing and/or treating cancer is crucial. More recently immunotherapy and gene therapy approaches utilizing antibodies and T-lymphocytes have emerged as new and promising methods for treating cancer.

[0048] Major histocompatibility complex (MHC) molecules, designated human leukocyte antigen (HLA) in humans, play a critical role in the body's recognition of disease and the resulting immune response to cancer and invading antigens. The HLA gene family is divided into two subgroups namely HLA Class I (HLA-I) and HLA Class II (HLA-II), with HLA-I further divided into classical HLA-I and non-classical HLA-I. Each HLA molecule forms a complex with one peptide from within the cell. On cancer cells, some of the peptide/HLA complexes are uniquely presented which enables

the immune system to recognize and kill these cells. Cells decorated with these unique peptide/HLA complexes are recognized and killed by the cytotoxic T cells (CTLs). Cancer cells show a downregulation in classical HLA-I expression but an upregulation in non-classical HLA-I expression (e.g. HLA-E). Thus, the upregulated uniquely presented non-classical HLA-I-peptide complexes on cancer cells are novel targets for developing innovative immunotherapies for treatment of cancer.

Certain terminology

[0049] Unless defined otherwise, all technical and scientific terms used herein have the same meaning as is commonly understood by one of skill in the art to which the claimed subject matter belongs. It is to be understood that the foregoing general description and the following detailed description are exemplary and explanatory only and are not restrictive of any subject matter claimed. The section headings used herein are for organizational purposes only and are not to be construed as limiting the subject matter described.

[0050] As used herein, singular forms “a”, “and,” and “the” include plural referents unless the context clearly indicates otherwise. Thus, for example, reference to “an antibody” includes a plurality of antibodies and reference to “an antibody” in some embodiments includes multiple antibodies, and so forth.

[0051] As used herein, all numerical values or numerical ranges include whole integers within or encompassing such ranges and fractions of the values or the integers within or encompassing ranges unless the context clearly indicates otherwise. Thus, for example, reference to a range of 90-100%, includes 91%, 92%, 93%, 94%, 95%, 95%, 97%, etc., as well as 91.1%, 91.2%, 91.3%, 91.4%, 91.5%, etc., 92.1%, 92.2%, 92.3%, 92.4%, 92.5%, etc., and so forth. In another example, reference to a range of 1-5,000 fold includes 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, fold, etc., as well as 1.1, 1.2, 1.3, 1.4, 1.5, fold, etc., 2.1, 2.2, 2.3, 2.4, 2.5, fold, etc., and so forth.

[0052] “About” a number, as used herein, refers to range including the number and ranging from 10% below that number to 10% above that number. “About” a range refers to 10% below the lower limit of the range, spanning to 10% above the upper limit of the range.

[0053] As used herein, the term “MHC” refers to the Major Histocompatibility Complex, which is a set of gene loci specifying major histocompatibility antigens. The term “HLA” as used herein refer to Human Leukocyte Antigens, which are the histocompatibility antigens found in humans. As used herein, “HLA” is the human form of “MHC” and the terms are used interchangeably.

[0054] As used herein “antibody” refers to a glycoprotein which exhibits binding specificity to a specific antigen. Antibodies herein also include “antigen binding portion” or fragments of the

antibody that are capable of binding to the antigen. The term includes, but is not limited to, polyclonal, monoclonal, monospecific, multispecific (e.g., bispecific antibodies), natural, humanized, human, chimeric, synthetic, recombinant, hybrid, mutated, grafted, antibody fragments (e.g., a portion of a full-length antibody, generally the antigen binding or variable region thereof, e.g., Fab, Fab', F(ab')₂, and Fv fragments), and *in vitro* generated antibodies so long as they exhibit the desired biological activity. The term also includes single chain antibodies, e.g., single chain Fv (sFv or scFv) antibodies, in which a variable heavy and a variable light chain are joined together (directly or through a peptide linker) to form a continuous polypeptide.

[0055] As used herein "CDR" refers to an immunoglobulin (Ig) hypervariable domain. A CDR is defined by any suitable manner. In some embodiments, CDRs can be defined in accordance with any of the Chothia numbering schemes, the Kabat numbering scheme, a combination of Kabat and Chothia, the AbM definition, the contact definition, and/or a combination of the Kabat, Chothia, AbM, and/or contact definitions; and may produce different results.

[0056] As used herein, the term "selectively binds" in the context of any binding agent, e.g., an antibody, refers to a binding agent that binds specifically to an antigen or epitope, such as with a high affinity, and does not significantly bind other unrelated antigens or epitopes.

[0057] As used herein the term "neoantigen" or "neopeptide" are used interchangeably and refer to a peptide differentially expressed by a diseased or stressed cell (e.g. cancer cell) compared to a healthy cell.

[0058] The terms "recipient", "individual", "subject", "host", and "patient", are used interchangeably herein and in some cases, refer to any mammalian subject for whom diagnosis, treatment, or therapy is desired, particularly humans. None of these terms require the supervision of medical personnel.

[0059] As used herein, the terms "treatment," "treating," and the like, in some cases, refer to administering an agent, or carrying out a procedure, for the purposes of obtaining an effect. The effect may be prophylactic in terms of completely or partially preventing a disease or symptom thereof and/or may be therapeutic in terms of effecting a partial or complete cure for a disease and/or symptoms of the disease. "Treatment," as used herein, may include treatment of a disease or disorder (e.g. cancer) in a mammal, particularly in a human, and includes: (a) preventing the disease or a symptom of a disease from occurring in a subject which may be predisposed to the disease but has not yet been diagnosed as having it (e.g., including diseases that may be associated with or caused by a primary disease; (b) inhibiting the disease, i.e., arresting its development; and (c)

relieving the disease, i.e., causing regression of the disease. Treating may refer to any indicia of success in the treatment or amelioration or prevention of a cancer, including any objective or subjective parameter such as abatement; remission; diminishing of symptoms or making the disease condition more tolerable to the patient; slowing in the rate of degeneration or decline; or making the final point of degeneration less debilitating. The treatment or amelioration of symptoms is based on one or more objective or subjective parameters; including the results of an examination by a physician. Accordingly, the term "treating" includes the administration of the compounds or agents of the present invention to prevent or delay, to alleviate, or to arrest or inhibit development of the symptoms or conditions associated with diseases (e.g. cancer). The term "therapeutic effect" refers to the reduction, elimination, or prevention of the disease, symptoms of the disease, or side effects of the disease in the subject.

[0060] A "therapeutically effective amount" in some cases means the amount that, when administered to a subject for treating a disease, is sufficient to effect treatment for that disease.

[0061] "Percent (%) identity" refers to the extent to which two sequences (nucleotide or amino acid) have the same residue at the same positions in an alignment. For example, "an amino acid sequence is X% identical to SEQ ID NO: Y" refers to % identity of the amino acid sequence to SEQ ID NO: Y and is elaborated as X% of residues in the amino acid sequence are identical to the residues of sequence disclosed in SEQ ID NO: Y. Generally, computer programs are employed for such calculations. Exemplary programs that compare and align pairs of sequences, include ALIGN (Myers and Miller, 1988), FASTA (Pearson and Lipman, 1988; Pearson, 1990) and gapped BLAST (Altschul et al., 1997), BLASTP, BLASTN, or GCG (Devereux et al., 1984).

Major Histocompatibility Complex (MHC) or Human Leukocyte Antigens (HLA)

[0062] Major histocompatibility complexes (MHC), also termed Human Leukocyte Antigens (HLA) in humans are glycoproteins expressed on the surface of nucleated cells that act as proteomic scanning chips by providing insight into the status of cellular health. They continuously sample peptides from normal host cellular proteins, cancer cells, inflamed cells and bacterial, viral and parasite infected cells and present short peptides on the surface of cells for recognition by T lymphocytes. Presented peptides can also be derived from proteins that are out of frame or from sequences embedded in the introns, or from proteins whose translation is initiated at codons other than the conventional methionine codon, ATG.

[0063] There are two classes of MHCs in mice and humans, namely MHC I and MHC II. MHC I comprises classical and non-classical MHC I sub-groups.

Classical MHC I or HLA-I

[0064] Classical MHC I molecules include HLA-A, HLA-B and HLA-C in humans and H-2-K, H-2-D, H-2-B and H-2-L in mice. Classical MHC I molecules are highly polymorphic with more than 2,735 alleles of HLA-A, 3,455 alleles of HLA-B and 2,259 alleles of HLA-C. Classical MHC I is expressed on the surface of all nucleated cells and present peptides to CD8 T lymphocytes. 30% of the proteins in the cellular machinery are rapidly degraded and are primary substrates for classical MHC I antigen presentation.

[0065] For peptide to be presented by classical MHC I molecules, proteins are first processed through the conventional processing route (ubiquitin proteasome system) which begins with protein degradation in the proteasome and Transporter associated protein (TAP) dependent transport of peptides into the endoplasmic reticulum (ER) and ends with the loading of peptides into the HLA peptide binding pocket. The proteins that contribute to the conventional processing route are collectively known as antigen processing machinery (APM) and include the proteasome, TAP complex, tapasin, endoplasmic reticulum amino peptidase (ERAAP), binding immunoglobulin protein (BiP), calnexin and calreticulin. Cells lacking either proteasome subunits, TAP1/2, ErP57 or calreticulin have reduced numbers of classical MHC I molecules on their surface.

Non-Classical MHC I or HLA-I

[0066] Non-classical MHC I molecules include HLA-E, HLA-F and HLA-G, and have limited polymorphisms. They play a role in regulating innate and adaptive immune responses. Non-classical MHC I molecules present peptides generated by both the conventional processing route and the alternative processing route in health and disease states, and represent a novel set of markers for targeting in disease states (e.g. cancer).

HLA-E

[0067] The non-classical MHC class I molecule, HLA-E is non-polymorphic. In nature, 13 HLA-E alleles have been identified with only two functional variants, namely HLA-E*0101 and HLA-E*0103. The difference between HLA-E*0101 (HLA-E^{107R}) and *0103 (HLA-E^{107G}) is a single amino acid difference at position 107 which is outside the peptide binding pocket. Similar to the classical MHC I molecules, HLA-E is expressed in all cells with a nucleus, however at usually lower levels. HLA-E molecule expression in cells and tissues is generally increased during stress and

disease. As such, HLA-E is differentially expressed on stressed or diseased cell (e.g. cancer cell) compared to on a healthy cell.

[0068] In healthy cells, it has been hypothesized that HLA-E presents peptides derived from classical MHC molecules to either inhibit or stimulate the activity of NK cells and a subset of CD8 T cells through engaging the receptor CD94/NKG2. Depending on the particular peptide presented by HLA-E, the HLA-E complex engages either CD94/NKG2A or CD94/NKG2C to inhibit or activate NK cells and a subset of CD8 T cells, respectively.

[0069] Another signal peptide that has characteristics in common with signal peptides generated from classical HLA-I molecules is the signal peptide generated from non-classical HLA-G. HLA-G expression under normal physiologic conditions is tightly regulated, with limited expression found in relatively few tissues and cells in the body. HLA-G plays a key role as an immune tolerant molecule and its expression is observed in cancer tissue/cells. Moreover, the signal peptide from HLA-G is processed by the conventional antigen processing pathway and delivered to the endoplasmic reticulum by the peptide transporter TAP. In some embodiments, the signal peptide is VMAPRTLFL (SEQ ID NO: 18).

[0070] HLA-E expression and peptide presentation in cancer cells

[0071] Cells deficient in one or more components of the APM load peptides into MHC class I molecules via alternative processing routes which are independent of the APM-dependent conventional processing route. APM-deficient cells not only have reduced numbers of classical MHC I molecules on their surface, but also show an increase in the cell surface density of HLA-E molecules as well as an increase in the repertoire of peptides presented. The alternative processing routes are constitutively turned on and produce peptides in both healthy and diseased cells. These peptides, however, are not presented by healthy cells; instead they are only presented in diseased or stressed cells. As such, the different peptide repertoires generated by APM-defective cells, also known as “T-cell epitopes associated with impaired peptide processing” (TEIPP), represent novel targets unique to cancer cells, and represent ideal targets for therapeutic development in the treatment of cancer.

[0072] In a stressed or diseased state (e.g. cancer), the stressed or diseased cell (e.g. a cancer cell) differentially expresses a complex comprising an HLA-E and a peptide derived from classical MHC molecules or the non-classical HLA-G molecule. The complex comprising an HLA-E and a peptide derived from classical MHC molecules or the non-classical HLA-G molecule is differentially expressed on the stressed or diseased cell compared to a healthy cell. Targeting this complex blocks

the inhibitory interaction of the complex with receptors on NK cells and a subset of CD8 T cells, thereby inducing an immune response against the cell expressing the complex.

MHC II or HLA-II

[0073] MHC II molecules in humans include HLA-DM, HLA-DO, HLA-DP, HLA-DQ and HLA-DR and include H-2 I-A and H-2 I-E in mice. MHC II expression is more restricted to B cells, dendritic cells, macrophages, activated T cells and thymic epithelial cells and MHC II molecules present peptides to CD4 lymphocytes.

Antibodies that target a complex comprising a non-classical HLA-I (e.g. HLA-E) and a neoantigen

[0074] Disclosed herein, in certain embodiments, are antibodies that target a complex comprising a non-classical HLA-I (e.g. HLA-E) and a neoantigen. In some embodiments, the antibodies comprise at least one heavy chain comprising a heavy chain variable domain (VH) and at least one light chain comprising a light chain variable domain (VL). Each VH and VL comprises three complementarity determining regions (CDR). The amino acid sequences of the VH and VL and the CDRs determine the antigen binding specificity and antigen binding strength of the antibody. The amino acid sequences of the VH and VL and the CDRs are summarized in Table 1.

Table 1. Antibodies

Human monoclonal antibody sequences that bind a complex comprising HLA-E and classical HLA signal peptides (ABX-0020, 0021, 0022,0023)		
	SEQUENCE	SEQ ID NO:
Light Chain CDR1	QSISSY	1
Light Chain CDR2	AAS	2
Light Chain CDR3	QQSATYWDM	3
Heavy Chain CDR1	GFTFSSYA	4
Heavy Chain CDR2	IAYGGGAT	5
Heavy Chain CDR3	AKGLSNFDY	6
Light Chain Variable domain	DIQMTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPG KAPKLLIYAASSLQSGVPSRFSGSGSGTDFTLTISLQPEDFA	7

	TYYCQQSATYWDMFGQGTKVEIKR	
Heavy Chain Variable domain	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQA PGKGLEWVSTIAYGGGATAYADSVKGRFTISRDN SKNTLY LQMNSLRAEDTAVYYCAKGLSNFDYWGQGT LVT VSS	8
Heavy Chain (human IgG1)	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQA PGKGLEWVSTIAYGGGATAYADSVKGRFTISRDN SKNTLY LQMNSLRAEDTAVYYCAKGLSNFDYWGQGT LVT VSSAST KGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVT VSWNSG ALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVN HKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFP PKPKDTLMISRTPEVTCVVDVSHEDPEVKFNWYVDGVEV HNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKV SNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSL TCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFL YSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPG K	30
Light Chain (human kappa)	DIQMTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPG KAPKLLIYAASSLQSGVPSRFSGSGSGTDFTLTISSLQPEDFA TYYCQQSATYWDMFGQGTKVEIKRTVAAPS VFIFPPSDEQL KSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVT EQDSKDDSTYLSSTLTLSKADYEKHKVYACEVTHQGLSSPV TKSFNRGEC	31
Heavy Chain (human IgG1) with ablation of FcγR binding with LALA mutation (Leu234Ala/Leu235Al)	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQA PGKGLEWVSTIAYGGGATAYADSVKGRFTISRDN SKNTLY LQMNSLRAEDTAVYYCAKGLSNFDYWGQGT LVT VSSAST KGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVT VSWNSG ALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVN HKPSNTKVDKKVEPKSCDKTHTCPPCPAPEAAGGPSVFLFP PKPKDTLMISRTPEVTCVVDVSHEDPEVKFNWYVDGVEV HNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKV SNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSL TCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFL YSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPG	32

	K	
Heavy Chain (human IgG1) with enhanced FcγR binding with DLE mutation (Ser239Asp/Ala330Leu/ Ile332Glu)	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQA PGKGLEWVSTIAYGGGATAYADSVKGRFTISRDN SKNTLY LQMNSLRAEDTAVYYCAKGLSNFDYWGQGT LVTVSSAST KGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVT VSWNSG ALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVN HKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPDVFLFP PKPKDTLMISRTPEVTCVVDVSHEDPEVKFNWYVDGVEV HNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKV SNKALPPLPEEKTKISKAKGQPREPQVYTLPPSREEMTKNQVS LTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFF LYSKLTVDKSRWQQGNV FSCSV MHEALHNHYTQKSLSLSP GK	33
Heavy Chain (mouse IgG1)	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQA PGKGLEWVSTIAYGGGATAYADSVKGRFTISRDN SKNTLY LQMNSLRAEDTAVYYCAKGLSNFDYWGQGT LVTVSSAKT TPPSVYPLAPGSAAQTNSMVTLGCLVKGYFPEPVT VTNWS GSLSSGVHTFPAVLQSDLYTLSSSVTVPSSPRPSETVTCNVA HPASSTKVDKKIVPRDCGCKPCICTVPEVSSVFIFPPKPKDV LTTITLTPKVTCVVDISKDDPEVQFSWFVDDVEVHTAQTQP REEQFNSTFRSVSELPIMHQDWLNGKEFKCRVNSAAFPAPI EKTISKTKGRPKAPQVYTIPPPKEQMAKDKVSLTCMITDFFP EDITVEWQWNGQPAENYKNTQPIMNTNGSYFVYSKLVNQ KSNWEAGNTFTCSVLHEGLHNHHTKSLSHSPGK	34
Light Chain (mouse kappa)	DIQMTQSPSSLSASVGDRTITCRASQSISSYLNWYQQKPG KAPKLLIYAASSLQSGVPSRFSGSGSGTDFTLTISLQPEDFA TYYCQQSATYWDMFGQGTKVEIKRADAAPTVSIFPPSSEQL TSGGASVVCFLNNFYPKDINVKWKIDGSERQNGVLNSWTD QDSKDSYMSSTLT LTKDEYERHNSYTCEATHKTSTSPIV KSFNRNEC	35
Mouse monoclonal antibody sequences binding CD3		
Light Chain CDR1	TGAVTTSNY	9

Light Chain CDR2	GTN	10
Light Chain CDR3	ALWYSNLWV	11
Heavy Chain CDR1	GFTFNTYA	12
Heavy Chain CDR2	IRSKYNNYAT	13
Heavy Chain CDR3	VRHGNFGNSYVSWFAY	14
Light Chain Variable domain	QAVVTQESALTTSPGETVTLTCRSSTGAVTTSNYANWVQE KPDHLFTGLIGGTNKRAPGVPARFSGSLIGDKAALTITGAQT EDEAIYFCALWYSNLWVFGGGTKLTVL	15
Heavy Chain Variable domain	EVQLVESGGGLVQPKGSLKLSCAASGFTFNTYAMNWRQ APGKGLEWVARIRSKYNNYATYYADSVKDRFTISRDDSQSI LYLQMNNLKTEDTAMYYCVRHGNFGNSYVSWFAYWGQG TLVTVSS	16

[0075] In some embodiments, the antibodies selectively bind to a complex comprising a non-classical HLA-I (e.g. HLA-E) and a neoantigen. In some embodiments, the antibody does not have a binding affinity to the non-classical HLA-I alone. In some embodiments, the antibody does not have a binding affinity to the neoantigen alone. In some embodiments, the antibody does not have a binding affinity to a complex comprising the non-classical HLA-I and a non-relevant neoantigen.

[0076] In some embodiments, the neoantigen is expressed by an antigen processing machinery (APM)-proficient cell. In some embodiments, the neoantigen is expressed by a TAP1/2-proficient cell. In some embodiments, the neoantigen comprises, consists essentially of, or consists of a sequence according to SEQ ID NO: 17 (VMAPRTLIL), SEQ ID NO: 18 (VMAPRTLFL), SEQ ID NO: 19 (VMAPRTLVL), SEQ ID NO: 20 (VTAPRTLIL), SEQ ID NO: 21 (IMAPRTLVL), SEQ ID NO: 23 (VMAQALLL), SEQ ID NO: 24 (VMAPRALLL), SEQ ID NO: 25 (VMAPRTLIL), SEQ ID NO: 26 (VMAPRTLTL), SEQ ID NO: 27 (VMAPRTVLL), SEQ ID NO: 28 (VMPRTLIL), or SEQ ID NO: 29 (VTAPRTLVL). In some embodiments, the neoantigen comprises, consists essentially of, or consists of a sequence according to SEQ ID NO: 17 (VMAPRTLIL), SEQ ID NO: 18 (VMAPRTLFL), SEQ ID NO: 19 (VMAPRTLVL), SEQ ID NO: 26 (VMAPRTLTL), or SEQ ID NO: 27 (VMAPRTVLL).

[0077] In some embodiments, the non-classical HLA-I is HLA-E, HLA-F, HLA-G, or HLA-H. In some embodiments, the non-classical HLA-I is HLA-E. In some embodiments, the HLA-E is HLA-E*0101. In some embodiments, the HLA-E is HLA-E*0103.

[0078] In some embodiments, the antibody selectively binds to the complex comprising the HLA-E and the neoantigen. In some embodiments, the antibody selectively binds to the complex comprising the HLA-E*0101 and the neoantigen. In some embodiments, the antibody selectively binds to the complex comprising the HLA-E*0103 and the neoantigen. In some embodiments, the antibody selectively binds to the complex comprising the HLA-E*0101 and the neoantigen, and to the complex of the HLA-E*0103 and the neoantigen. In some embodiments, the complex comprises the HLA-E and a neoantigen selected from the group consisting of: SEQ ID NO: 17 (VMAPRTLIL), SEQ ID NO: 18 (VMAPRTLFL), SEQ ID NO: 19 (VMAPRTLVL), SEQ ID NO: 20 (VTAPRTLIL), SEQ ID NO: 21 (IMAPRTLVL), SEQ ID NO: 23 (VMAQALIL), SEQ ID NO: 24 (VMAQALLL), SEQ ID NO: 25 (VMAQRTLIL), SEQ ID NO: 26 (VMAQRTLVL), SEQ ID NO: 27 (VMAQRTLVL), SEQ ID NO: 28 (VMPRTLIL), and SEQ ID NO: 29 (VTAPRTLVL). In some embodiments, the complex comprises the HLA-E and a neoantigen selected from the group consisting of: SEQ ID NO: 17 (VMAPRTLIL), SEQ ID NO: 18 (VMAPRTLFL), SEQ ID NO: 19 (VMAPRTLVL), SEQ ID NO: 26 (VMAQRTLVL), and SEQ ID NO: 27 (VMAQRTLVL).

[0079] In some embodiments, the antibody is a murine antibody. In some embodiments, the antibody is a chimeric antibody. In some embodiments, the antibody is a camelid antibody. In some embodiments, the antibody is a humanized antibody. In some embodiments, the antibody is a human antibody.

[0080] In some embodiments, the antibody is a TCR-like antibody. In some embodiments, the antibody is a single domain antibody. In some embodiments, the single domain antibody is a camelid single domain antibody.

[0081] In some embodiments, the antibody is a multispecific antibody. In some embodiments, the antibody is a bispecific antibody. In some embodiments, the antibody is a bispecific T cell engager (BiTE). In some embodiments, the BiTE binds to a CD3 protein associated with a T cell receptor (TCR). In some embodiments, the BiTE binds to a CD3ε protein associated with a T cell receptor (TCR). In some embodiments, the antibody is a multifunctional antibody.

[0082] In some embodiments, the antibody further comprises a conjugated therapeutic moiety. Therapeutic moiety include, but are not limited to, a cytotoxin, a chemotherapeutic drug, an immunosuppressant, and a radioisotope. A cytotoxin or cytotoxic agent includes any agent that is

detrimental to (e.g., kills) cells. Examples include, but are not limited to, taxol, cytochalasin B, gramicidin D, ethidium bromide, emetine, mitomycin, etoposide, teniposide, vincristine, vinblastine, colchicin, doxorubicin, daunorubicin, dihydroxy anthracin dione, mitoxantrone, mithramycin, actinomycin D, 1-dehydrotestosterone, glucocorticoids, procaine, tetracaine, lidocaine, propranolol, and puromycin and analogs or homologs thereof. Suitable chemotherapeutic agents include, but are not limited to, anti-metabolites (e.g., methotrexate, 6-mercaptopurine, 6-thioguanine, cytarabine, fludarabin, 5-fluorouracil, decarbazine, hydroxyurea, azathioprin, gemcitabin and cladribin), alkylating agents (e.g., mechlorethamine, thioepa, chlorambucil, melphalan, carmustine (BSNU) and lomustine (CCNU), cyclophosphamide, busulfan, dibromomannitol, streptozotocin, mitomycin C, and cis-dichlorodiamine platinum (II) (DDP) cisplatin), anthracyclines (e.g., daunorubicin (formerly daunomycin) and doxorubicin), antibiotics (e.g., dactinomycin (formerly actinomycin), bleomycin, mithramycin, and anthramycin (AMC)), and anti-mitotic agents (e.g., vincristine, vinblastine, docetaxel, paclitaxel and vinorelbin). Suitable radioisotopes include, but are not limited to, iodine-131, yttrium-90 or indium-111. Further examples of therapeutic moieties are a protein or polypeptide possessing a desired biological activity. Such proteins may include, for example, an enzymatically active toxin, or active fragment thereof, such as abrin, ricin A, pseudomonas exotoxin, or diphtheria toxin; a protein such as tumor necrosis factor or interferon- γ ; or biological response modifiers such as, for example, lymphokines, interleukin-1 (IL-1), interleukin-2 (IL-2), interleukin-6 (IL-6), granulocyte macrophage colony stimulating factor (GM-CSF), granulocyte colony stimulating factor (G-CSF), or other growth factors.

[0083] In some embodiments, the selective binding of the antibody to the complex comprising the non-classical HLA-I (e.g. HLA-E) and the neoantigen induces an immune response. In some embodiments, the immune response comprises activation of T cells. In some embodiments, the T cell is a CD8+ T cell. In some embodiments, the immune response comprises activation of cytotoxic T cells (CTLs). In some embodiments, the cell is a cancer cell.

Antibody Variable Domain (VL and VH)

[0084] Disclosed herein are antibodies that selectively bind to a complex comprising an HLA-E and a neoantigen, the antibodies having a light chain comprising a light chain variable domain (VL). In some embodiments, antibodies comprise a light chain variable domain (VL) having an amino acid sequence at least about 70% identical to an amino acid sequence set forth as SEQ ID NO: 7. In some embodiments the VL has an amino acid sequence at least about 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99%

identical to an amino acid sequence set forth as SEQ ID NO: 7. In some embodiments, the VL has an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 7.

[0085] Further disclosed herein are antibodies that selectively bind to a complex comprising an HLA-E and a neoantigen, the antibodies having a heavy chain comprising a heavy chain variable domain (VH). In some embodiments, antibodies comprise a heavy chain variable domain (VH) having an amino acid sequence at least about 70% identical to an amino acid sequence set forth as SEQ ID NO: 8. In some embodiments the VH has an amino acid sequence at least about 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 8. In some embodiments, the VH has an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 8.

[0086] Also disclosed herein are antibodies that selectively bind to a complex comprising an HLA-E and a neoantigen, the antibodies comprising a light chain variable domain (VL) and a heavy chain variable domain (VH). In some embodiments, antibodies comprise a light chain variable domain (VL) having an amino acid sequence at least about 70% identical to an amino acid sequence set forth as SEQ ID NO: 7 and a heavy chain variable domain (VH) having an amino acid sequence at least about 70% identical to an amino acid sequence set forth as SEQ ID NO: 8. In some embodiments the VL has an amino acid sequence at least about 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 7 and the VH has an amino acid sequence at least about 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 8. In some embodiments, the VL has an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 7 and the VH has an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 8.

Antibody heavy chain and light chain

[0087] Disclosed herein are antibodies that selectively bind to a complex comprising an HLA-E and a neoantigen, the antibodies having a light chain (LC). In some embodiments, antibodies comprise a light chain (LC) having an amino acid sequence at least about 70% identical to an amino acid sequence set forth as SEQ ID NO: 31. In some embodiments the LC has an amino acid sequence at least about 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO:

31. In some embodiments, the LC has an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 31.

[0088] Further disclosed herein are antibodies that selectively bind to a complex comprising an HLA-E and a neoantigen, the antibodies having a heavy chain (HC). In some embodiments, antibodies comprise a HC having an amino acid sequence at least about 70% identical to an amino acid sequence set forth as SEQ ID NO: 30. In some embodiments the HC has an amino acid sequence at least about 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 30. In some embodiments, the HC has an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 30.

[0089] Also disclosed herein are antibodies that selectively bind to a complex comprising an HLA-E and a neoantigen, the antibodies comprising a light chain (LC) and a heavy chain (HC). In some embodiments, antibodies comprise a LC having an amino acid sequence at least about 70% identical to an amino acid sequence set forth as SEQ ID NO: 31 and a HC having an amino acid sequence at least about 70% identical to an amino acid sequence set forth as SEQ ID NO: 30. In some embodiments the LC has an amino acid sequence at least about 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 31 and the HC has an amino acid sequence at least about 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 30. In some embodiments, the LC has an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 31 and the HC has an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 30.

[0090] Further disclosed herein are antibodies that selectively bind to a complex comprising an HLA-E and a neoantigen, the antibodies having a heavy chain (HC). In some embodiments, antibodies comprise a HC having an amino acid sequence at least about 70% identical to an amino acid sequence set forth as SEQ ID NO: 32. In some embodiments the HC has an amino acid sequence at least about 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 32. In some embodiments, the HC has an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 32.

[0091] Also disclosed herein are antibodies that selectively bind to a complex comprising an HLA-E and a neoantigen, the antibodies comprising a light chain (LC) and a heavy chain (HC). In some embodiments, antibodies comprise a LC having an amino acid sequence at least about 70% identical to an amino acid sequence set forth as SEQ ID NO: 31 and a HC having an amino acid sequence at least about 70% identical to an amino acid sequence set forth as SEQ ID NO: 32. In some embodiments the LC has an amino acid sequence at least about 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 31 and the HC has an amino acid sequence at least about 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 32. In some embodiments, the LC has an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 31 and the HC has an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 32.

[0092] Further disclosed herein are antibodies that selectively bind to a complex comprising an HLA-E and a neoantigen, the antibodies having a heavy chain (HC). In some embodiments, antibodies comprise a HC having an amino acid sequence at least about 70% identical to an amino acid sequence set forth as SEQ ID NO: 33. In some embodiments the HC has an amino acid sequence at least about 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 33. In some embodiments, the HC has an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 33.

[0093] Also disclosed herein are antibodies that selectively bind to a complex comprising an HLA-E and a neoantigen, the antibodies comprising a light chain (LC) and a heavy chain (HC). In some embodiments, antibodies comprise a LC having an amino acid sequence at least about 70% identical to an amino acid sequence set forth as SEQ ID NO: 31 and a HC having an amino acid sequence at least about 70% identical to an amino acid sequence set forth as SEQ ID NO: 33. In some embodiments the LC has an amino acid sequence at least about 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 31 and the HC has an amino acid sequence at least about 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 33. In some embodiments, the LC has an amino acid sequence 100% identical to an amino acid sequence

set forth as SEQ ID NO: 31 and the HC has an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 33.

[0094] Disclosed herein are antibodies that selectively bind to a complex comprising an HLA-E and a neoantigen, the antibodies having a light chain (LC). In some embodiments, antibodies comprise a light chain (LC) having an amino acid sequence at least about 70% identical to an amino acid sequence set forth as SEQ ID NO: 35. In some embodiments the LC has an amino acid sequence at least about 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 35. In some embodiments, the LC has an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 35.

[0095] Further disclosed herein are antibodies that selectively bind to a complex comprising an HLA-E and a neoantigen, the antibodies having a heavy chain (HC). In some embodiments, antibodies comprise a HC having an amino acid sequence at least about 70% identical to an amino acid sequence set forth as SEQ ID NO: 34. In some embodiments the HC has an amino acid sequence at least about 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 34. In some embodiments, the HC has an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 34.

[0096] Also disclosed herein are antibodies that selectively bind to a complex comprising an HLA-E and a neoantigen, the antibodies comprising a light chain (LC) and a heavy chain (HC). In some embodiments, antibodies comprise a LC having an amino acid sequence at least about 70% identical to an amino acid sequence set forth as SEQ ID NO: 35 and a HC having an amino acid sequence at least about 70% identical to an amino acid sequence set forth as SEQ ID NO: 34. In some embodiments the LC has an amino acid sequence at least about 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 35 and the HC has an amino acid sequence at least about 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 34. In some embodiments, the LC has an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 35 and the HC has an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 34.

Antibody Complementarity Determining Regions (CDR)

[0097] Disclosed herein are antibodies that selectively bind to a complex comprising an HLA-E and a neoantigen, the antibodies having a light chain comprising a light chain complementarity determining region (CDR). In some embodiments, antibodies comprise a light chain CDR sequence having an amino acid sequence at least about 70% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 1-3. In some embodiments, antibodies comprise a light chain CDR sequence having an amino acid sequence at least about 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 1-3. In some embodiments, antibodies comprise a light chain CDR sequence having an amino acid sequence 100% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 1-3.

[0098] Further disclosed herein are antibodies that selectively bind to a complex comprising an HLA-E and a neoantigen, the antibodies having a heavy chain comprising a heavy chain complementarity determining region (CDR). In some embodiments, antibodies comprise a heavy chain CDR sequence having an amino acid sequence at least about 70% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6. In some embodiments, antibodies comprise a heavy chain CDR sequence having an amino acid sequence at least about 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6. In some embodiments, antibodies comprise a heavy chain CDR sequence having an amino acid sequence 100% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6.

[0099] Also disclosed herein are antibodies that selectively bind to a complex comprising an HLA-E and a neoantigen comprise a light chain complementarity determining region (CDR) and a heavy chain complementarity determining region (CDR). In some embodiments, antibodies comprise a light chain CDR sequence having an amino acid sequence at least about 70% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 1-3 and a heavy chain CDR sequence having an amino acid sequence at least about 70% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6. In some embodiments, antibodies comprise a light chain CDR sequence having an amino acid sequence at least about 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 1-3 and a heavy chain CDR sequence having an amino acid sequence at least about 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%,

90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6. In some embodiments, antibodies comprise a light chain CDR sequence having an amino acid sequence 100% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 1-3 and a heavy chain CDR sequence having an amino acid sequence at least about 100% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6.

[00100] In some embodiments, antibodies selectively bind to a complex comprising an HLA-E and a neoantigen comprise at least one of a light chain CDR1 having an amino acid sequence at least about 70% identical to an amino acid sequence set forth as SEQ ID NO: 1, a light chain CDR2 having an amino acid sequence at least about 70% identical to an amino acid sequence set forth as SEQ ID NO: 2, and a light chain CDR3 having an amino acid sequence at least about 70% identical to an amino acid sequence set forth as SEQ ID NO: 3. In some embodiments, antibodies comprise at least one of a light chain a light chain CDR1 having an amino acid sequence at least about 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 1, a light chain CDR2 having an amino acid sequence at least about 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 2, and a light chain CDR3 having an amino acid sequence at least about 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 3. In some embodiments, antibodies comprise at least one of a light chain CDR1 having an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 1, a light chain CDR2 having an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 2, and a light chain CDR3 having an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 3.

[00101] In some embodiments, antibodies that selectively bind to a complex comprising an HLA-E and a neoantigen comprise at least one of a heavy chain CDR1 having an amino acid sequence at least about 70% identical to an amino acid sequence set forth as SEQ ID NO: 4, a heavy chain CDR2 having an amino acid sequence at least about 70% identical to an amino acid sequence set forth as SEQ ID NO: 5, a heavy chain CDR3 having an amino acid sequence at least about 70% identical to an amino acid sequence set forth as SEQ ID NO: 6. In some embodiments, antibodies comprise at least one of a heavy chain CDR1 having an amino acid sequence at least about 75%,

80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 4, a heavy chain CDR2 having an amino acid sequence at least about 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 5, a heavy chain CDR3 having an amino acid sequence at least about 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 6. In some embodiments, antibodies comprise at least one of a heavy chain CDR1 having an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 4, a heavy chain CDR2 having an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 5, a heavy chain CDR3 having an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 6.

[00102] In some embodiments, antibodies that selectively bind to a complex comprising an HLA-E and a neoantigen comprise at least one of a light chain CDR1 having an amino acid sequence at least about 70% identical to an amino acid sequence set forth as SEQ ID NO: 1, a light chain CDR2 having an amino acid sequence at least about 70% identical to an amino acid sequence set forth as SEQ ID NO: 2, a light chain CDR3 having an amino acid sequence at least about 70% identical to an amino acid sequence set forth as SEQ ID NO: 3, a heavy chain CDR1 having an amino acid sequence at least about 70% identical to an amino acid sequence set forth as SEQ ID NO: 4, a heavy chain CDR2 having an amino acid sequence at least about 70% identical to an amino acid sequence set forth as SEQ ID NO: 5, and a heavy chain CDR3 having an amino acid sequence at least about 70% identical to an amino acid sequence set forth as SEQ ID NO: 6. In some embodiments, antibodies comprise at least one of a light chain CDR1 having an amino acid sequence at least about 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 1, a light chain CDR2 having an amino acid sequence at least about 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 2, a light chain CDR3 having an amino acid sequence at least about 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 3, a heavy chain CDR1 having an amino acid sequence at least about 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or

99% identical to an amino acid sequence set forth as SEQ ID NO: 4, a heavy chain CDR2 having an amino acid sequence at least about 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 5, and a heavy chain CDR3 having an amino acid sequence at least about 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 6. In some embodiments, antibodies comprise at least one of a light chain CDR1 having an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 1, a light chain CDR2 having an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 2, a light chain CDR3 having an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 3, a heavy chain CDR1 having an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 4, a heavy chain CDR2 having an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 5, and a heavy chain CDR3 having an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 6.

Bispecific antibodies

[00103] In some embodiments, the antibodies disclosed herein are bispecific antibodies. In some embodiments, the bispecific antibodies are bispecific T cell engagers (BiTEs). In some embodiments, the BiTE binds to a CD3 protein associated with a T cell receptor (TCR). In some embodiments, the BiTE binds to a CD3ε protein associated with a T cell receptor (TCR).

[00104] In some embodiments, the BiTE comprises an anti-CD3 antibody, or a fragment thereof, such as UCHT1, OKT3, F6A, L2K, muromonab, oteelixizumab, teplizumab, visilizumab, CD3-12, MEM-57, 4D10A6, CD3D, or TR66.

[00105] In some embodiments, the bispecific antibodies comprise (a) a light chain variable domain (VL) comprising an amino acid sequence at least 70% identical to an amino acid sequence set forth as SEQ ID NO: 7; or a heavy chain variable domain (VH) comprising an amino acid sequence at least 70% identical to an amino acid sequence set forth as SEQ ID NO: 8; and (b) a light chain variable domain (VL) comprising an amino acid sequence at least 70% identical to an amino acid sequence set forth as SEQ ID NO: 15; or a heavy chain variable domain (VH) comprising an amino acid sequence at least 70% identical to an amino acid sequence set forth as SEQ ID NO: 16.

[00106] In some embodiments, the bispecific antibodies comprise (a) a light chain variable domain (VL) comprising an amino acid sequence at least 75%, 80%, 81%, 82%, 83%, 84%, 85%,

86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 7; or a heavy chain variable domain (VH) comprising an amino acid sequence at least 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 8; and (b) a light chain variable domain (VL) comprising an amino acid sequence at least 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 15; or a heavy chain variable domain (VH) comprising an amino acid sequence at least 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 16.

[00107] In some embodiments, the bispecific antibodies comprise (a) a light chain variable domain (VL) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 7; or a heavy chain variable domain (VH) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 8; and (b) a light chain variable domain (VL) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 15; or a heavy chain variable domain (VH) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 16.

[00108] In some embodiments, the bispecific antibodies comprise (a) a light chain variable domain (VL) comprising an amino acid sequence at least 70% identical to an amino acid sequence set forth as SEQ ID NO: 7; and a heavy chain variable domain (VH) comprising an amino acid sequence at least 70% identical to an amino acid sequence set forth as SEQ ID NO: 8; and (b) a light chain variable domain (VL) comprising an amino acid sequence at least 70% identical to an amino acid sequence set forth as SEQ ID NO: 15; and a heavy chain variable domain (VH) comprising an amino acid sequence at least 70% identical to an amino acid sequence set forth as SEQ ID NO: 16.

[00109] In some embodiments, the bispecific antibodies comprise (a) a light chain variable domain (VL) comprising an amino acid sequence at least 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 7; and a heavy chain variable domain (VH) comprising an amino acid sequence at least 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 8; and (b) a light chain variable domain (VL) comprising an amino acid sequence at least 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%,

91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 15; and a heavy chain variable domain (VH) comprising an amino acid sequence at least 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 16.

[00110] In some embodiments, the bispecific antibodies comprise (a) a light chain variable domain (VL) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 7; and a heavy chain variable domain (VH) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 8; and (b) a light chain variable domain (VL) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 15; and a heavy chain variable domain (VH) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 16.

[00111] In some embodiments, the bispecific antibodies comprise (a) a light chain (LC) comprising an amino acid sequence at least 70% identical to an amino acid sequence set forth as SEQ ID NO: 31; or a heavy chain (HC) comprising an amino acid sequence at least 70% identical to an amino acid sequence set forth as SEQ ID NO: 30; and (b) a light chain variable domain (VL) comprising an amino acid sequence at least 70% identical to an amino acid sequence set forth as SEQ ID NO: 15; or a heavy chain variable domain (VH) comprising an amino acid sequence at least 70% identical to an amino acid sequence set forth as SEQ ID NO: 16.

[00112] In some embodiments, the bispecific antibodies comprise (a) a light chain (LC) comprising an amino acid sequence at least 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 31; or a heavy chain (HC) comprising an amino acid sequence at least 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 30; and (b) a light chain variable domain (VL) comprising an amino acid sequence at least 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 15; or a heavy chain variable domain (VH) comprising an amino acid sequence at least 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 16.

[00113] In some embodiments, the bispecific antibodies comprise (a) a light chain (LC) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID

NO:31; or a heavy chain (HC) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 30; and (b) a light chain variable domain (VL) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 15; or a heavy chain variable domain (VH) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 16.

[00114] In some embodiments, the bispecific antibodies comprise (a) a light chain (LC) comprising an amino acid sequence at least 70% identical to an amino acid sequence set forth as SEQ ID NO:31; or a heavy chain (HC) comprising an amino acid sequence at least 70% identical to an amino acid sequence set forth as SEQ ID NO: 32; and (b) a light chain variable domain (VL) comprising an amino acid sequence at least 70% identical to an amino acid sequence set forth as SEQ ID NO: 15; or a heavy chain variable domain (VH) comprising an amino acid sequence at least 70% identical to an amino acid sequence set forth as SEQ ID NO: 16.

[00115] In some embodiments, the bispecific antibodies comprise (a) a light chain (LC) comprising an amino acid sequence at least 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 31; or a heavy chain (HC) comprising an amino acid sequence at least 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 32; and (b) a light chain variable domain (VL) comprising an amino acid sequence at least 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 15; or a heavy chain variable domain (VH) comprising an amino acid sequence at least 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 16.

[00116] In some embodiments, the bispecific antibodies comprise (a) a light chain (LC) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO:31; or a heavy chain (HC) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 32; and (b) a light chain variable domain (VL) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 15; or a heavy chain variable domain (VH) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 16.

[00117] In some embodiments, the bispecific antibodies comprise (a) a light chain (LC) comprising an amino acid sequence at least 70% identical to an amino acid sequence set forth as SEQ ID NO:31; or a heavy chain (HC) comprising an amino acid sequence at least 70% identical to an amino acid sequence set forth as SEQ ID NO: 33; and (b) a light chain variable domain (VL) comprising an amino acid sequence at least 70% identical to an amino acid sequence set forth as SEQ ID NO: 15; or a heavy chain variable domain (VH) comprising an amino acid sequence at least 70% identical to an amino acid sequence set forth as SEQ ID NO: 16.

[00118] In some embodiments, the bispecific antibodies comprise (a) a light chain (LC) comprising an amino acid sequence at least 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 31; or a heavy chain (HC) comprising an amino acid sequence at least 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 33; and (b) a light chain variable domain (VL) comprising an amino acid sequence at least 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 15; or a heavy chain variable domain (VH) comprising an amino acid sequence at least 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 16.

[00119] In some embodiments, the bispecific antibodies comprise (a) a light chain (LC) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO:31; or a heavy chain (HC) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 33; and (b) a light chain variable domain (VL) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 15; or a heavy chain variable domain (VH) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 16.

[00120] In some embodiments, the bispecific antibodies comprise (a) a light chain (LC) comprising an amino acid sequence at least 70% identical to an amino acid sequence set forth as SEQ ID NO:35; or a heavy chain (HC) comprising an amino acid sequence at least 70% identical to an amino acid sequence set forth as SEQ ID NO: 34; and (b) a light chain variable domain (VL) comprising an amino acid sequence at least 70% identical to an amino acid sequence set forth as

SEQ ID NO: 15; or a heavy chain variable domain (VH) comprising an amino acid sequence at least 70% identical to an amino acid sequence set forth as SEQ ID NO: 16.

[00121] In some embodiments, the bispecific antibodies comprise (a) a light chain (LC) comprising an amino acid sequence at least 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 35; or a heavy chain (HC) comprising an amino acid sequence at least 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 34; and (b) a light chain variable domain (VL) comprising an amino acid sequence at least 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 15; or a heavy chain variable domain (VH) comprising an amino acid sequence at least 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 16.

[00122] In some embodiments, the bispecific antibodies comprise (a) a light chain (LC) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 35; or a heavy chain (HC) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 34; and (b) a light chain variable domain (VL) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 15; or a heavy chain variable domain (VH) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 16.

[00123] In some embodiments, the bispecific antibodies comprise (a) a light chain complementarity determining region (CDR) having an amino acid sequence at least 70% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 1-3; or a heavy chain complementarity determining region (CDR) having an amino acid sequence at least 70% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6; and (b) a light chain complementarity determining region (CDR) having an amino acid sequence at least 70% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 9-11; or a heavy chain complementarity determining region (CDR) having an amino acid sequence at least 70% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 12-14.

[00124] In some embodiments, the bispecific antibodies comprise (a) a light chain complementarity determining region (CDR) having an amino acid sequence at least 75%, 80%, 81%,

82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 1-3; or a heavy chain complementarity determining region (CDR) having an amino acid sequence at least 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6; and (b) a light chain complementarity determining region (CDR) having an amino acid sequence at least 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 9-11; or a heavy chain complementarity determining region (CDR) having an amino acid sequence at least 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 12-14.

[00125] In some embodiments, the bispecific antibodies comprise (a) a light chain complementarity determining region (CDR) having an amino acid sequence 100% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 1-3; or a heavy chain complementarity determining region (CDR) having an amino acid sequence 100% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6; and (b) a light chain complementarity determining region (CDR) having an amino acid sequence 100% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 9-11; or a heavy chain complementarity determining region (CDR) having an amino acid sequence 100% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 12-14.

[00126] In some embodiments, the bispecific antibodies comprise (a) a light chain complementarity determining region (CDR) having an amino acid sequence at least 70% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 1-3; and a heavy chain complementarity determining region (CDR) having an amino acid sequence at least 70% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6; and (b) a light chain complementarity determining region (CDR) having an amino acid sequence at least 70% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 9-11; and a heavy chain complementarity determining region (CDR) having an amino acid sequence at least 70% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 12-14.

[00127] In some embodiments, the bispecific antibodies comprise (a) a light chain complementarity determining region (CDR) having an amino acid sequence at least 75%, 80%, 81%,

82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 1-3; and a heavy chain complementarity determining region (CDR) having an amino acid sequence at least 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6; and (b) a light chain complementarity determining region (CDR) having an amino acid sequence at least 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 9-11; and a heavy chain complementarity determining region (CDR) having an amino acid sequence at least 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 12-14.

[00128] In some embodiments, the bispecific antibodies comprise (a) a light chain complementarity determining region (CDR) having an amino acid sequence 100% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 1-3; and a heavy chain complementarity determining region (CDR) having an amino acid sequence 100% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6; and (b) a light chain complementarity determining region (CDR) having an amino acid sequence 100% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 9-11; and a heavy chain complementarity determining region (CDR) having an amino acid sequence 100% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 12-14.

Methods of Treatment

[00129] Provided herein are methods of treating cancer in an individual in need thereof comprising administering to the individual an antibody that selectively bind to a complex comprising a non-classical HLA-I (e.g. HLA-E) and a neoantigen as disclosed herein.

[00130] In some embodiments, the cancer is breast cancer. In some embodiments, the cancer is kidney cancer. In some embodiments, the cancer is lung cancer. In some embodiments, the cancer is ovarian cancer. In some embodiments, the cancer is colorectal cancer. In some embodiments, the cancer is pancreatic cancer. In some embodiments, the cancer is choriocarcinoma. In some embodiments, the cancer is non-small cell lung carcinoma (NSCLC). In some embodiments, the cancer is gastric cancer. In some embodiments, the cancer is cervical cancer. In some embodiments,

the cancer is head and neck cancer. In some embodiments, the cancer is a myeloma. In some embodiments, the cancer is a leukemia. In some embodiments, the cancer is a lymphoma. In some embodiments, the cancer is acute myeloid leukemia (AML). In some embodiments, the cancer is multiple myeloma. In some embodiments, the cancer is a myelodysplastic syndrome. In some embodiments, the cancer is a B-cell malignancy. In some embodiments, the cancer is mantle cell lymphoma.

[00131] In some embodiments, the cancer cell differentially expresses the neoantigen. In some embodiments, the cancer cell differentially expresses the HLA-E. In some embodiments, the cancer cell differentially expresses the complex comprising the HLA-E and the neoantigen.

[00132] In some embodiments, the antibody selectively bind to a complex comprising a non-classical HLA-I (e.g. HLA-E) and a neoantigen. In some embodiments, the antibody does not have a binding affinity to the non-classical HLA-I alone. In some embodiments, the antibody does not have a binding affinity to the neoantigen alone. In some embodiments, the antibody does not have a binding affinity to a complex comprising the non-classical HLA-I and a non-relevant neoantigen.

[00133] In some embodiments, the neoantigen is expressed by an antigen processing machinery (APM)-proficient cell. In some embodiments, the neoantigen is expressed by a TAP1/2-proficient cell. In some embodiments, the neoantigen comprises, consists essentially of, or consists of a sequence according to SEQ ID NO: 17 (VMAPRTLIL), SEQ ID NO: 18 (VMAPRTLFL), SEQ ID NO: 19 (VMAPRTLVL), SEQ ID NO: 20 (VTAPRTLLL), SEQ ID NO: 21 (IMAPRTLVL), SEQ ID NO: 23 (VMAPQALLL), SEQ ID NO: 24 (VMAPRALLL), SEQ ID NO: 25 (VMAPRTLALL), SEQ ID NO: 26 (VMAPRTLTL), SEQ ID NO: 27 (VMAPRTVLL), SEQ ID NO: 28 (VMPPTLLL), or SEQ ID NO: 29 (VTAPRTVLL). In some embodiments, the neoantigen comprises, consists essentially of, or consists of a sequence according to SEQ ID NO: 17 (VMAPRTLIL), SEQ ID NO: 18 (VMAPRTLFL), SEQ ID NO: 19 (VMAPRTLVL), SEQ ID NO: 26 (VMAPRTLTL), or SEQ ID NO: 27 (VMAPRTVLL).

[00134] In some embodiments, the non-classical HLA-I is HLA-E, HLA-F, HLA-G, or HLA-H. In some embodiments, the non-classical HLA-I is HLA-E. In some embodiments, the HLA-E is HLA-E*0101. In some embodiments, the HLA-E is HLA-E*0103.

[00135] In some embodiments, the antibody selectively binds to the complex comprising the HLA-E and the neoantigen. In some embodiments, the antibody selectively binds to the complex comprising the HLA-E*0101 and the neoantigen. In some embodiments, the antibody selectively binds to the complex comprising the HLA-E*0103 and the neoantigen. In some embodiments, the

antibody selectively binds to the complex comprising the HLA-E*0101 and the neoantigen, and to the complex of the HLA-E*0103 and the neoantigen. In some embodiments, the complex comprises the HLA-E and a neoantigen selected from the group consisting of: SEQ ID NO: 17 (VMAPRTLIL), SEQ ID NO: 18 (VMAPRTLFL), SEQ ID NO: 19 (VMAPRTLVL), SEQ ID NO: 20 (VTAPRTLIL), SEQ ID NO: 21 (IMAPRTLVL), SEQ ID NO: 23 (VMAPQALLL), SEQ ID NO: 24 (VMAPRALLL), SEQ ID NO: 25 (VMAPRTLIL), SEQ ID NO: 26 (VMAPRTLTL), SEQ ID NO: 27 (VMAPRTVLL), SEQ ID NO: 28 (VMPPRTLIL), and SEQ ID NO: 29 (VTAPRTVLL). In some embodiments, the complex comprises the HLA-E and a neoantigen selected from the group consisting of: SEQ ID NO: 17 (VMAPRTLIL), SEQ ID NO: 18 (VMAPRTLFL), SEQ ID NO: 19 (VMAPRTLVL), SEQ ID NO: 26 (VMAPRTLTL), and SEQ ID NO: 27 (VMAPRTVLL).

[00136] In some embodiments, the antibody is a murine antibody. In some embodiments, the antibody is a chimeric antibody. In some embodiments, the antibody is a camelid antibody. In some embodiments, the antibody is a humanized antibody. In some embodiments, the antibody is a human antibody.

[00137] In some embodiments, the antibody is a TCR-like antibody. In some embodiments, the antibody is a single domain antibody. In some embodiments, the single domain antibody is a camelid single domain antibody.

[00138] In some embodiments, the antibody is a multispecific antibody. In some embodiments, the antibody is a bispecific antibody. In some embodiments, the antibody is a bispecific T cell engager (BiTE). In some embodiments, the BiTE binds to a CD3 protein associated with a T cell receptor (TCR). In some embodiments, the BiTE binds to a CD3ε protein associated with a T cell receptor (TCR). In some embodiments, the antibody is a multifunctional antibody.

[00139] In some embodiments, the antibody further comprises a conjugated therapeutic moiety. Therapeutic moiety include, but are not limited to, a cytotoxin, a chemotherapeutic drug, an immunosuppressant, and a radioisotope. A cytotoxin or cytotoxic agent includes any agent that is detrimental to (e.g., kills) cells. Examples include, but are not limited to, taxol, cytochalasin B, gramicidin D, ethidium bromide, emetine, mitomycin, etoposide, teniposide, vincristine, vinblastine, colchicin, doxorubicin, daunorubicin, dihydroxy anthracin dione, mitoxantrone, mithramycin, actinomycin D, 1-dehydrotestosterone, glucocorticoids, procaine, tetracaine, lidocaine, propranolol, and puromycin and analogs or homologs thereof. Suitable chemotherapeutic agents include, but are not limited to, anti-metabolites (e.g., methotrexate, 6-mercaptopurine, 6-thioguanine, cytarabine, fludarabine, 5-fluorouracil, decarbazine, hydroxyurea, azathioprine, gemcitabine and cladribine),

alkylating agents (e.g., mechlorethamine, thioepa, chlorambucil, melphalan, carmustine (BSNU) and lomustine (CCNU), cyclophosphamide, busulfan, dibromomannitol, streptozotocin, mitomycin C, and cis-dichlorodiamine platinum (II) (DDP) cisplatin), anthracyclines (e.g., daunorubicin (formerly daunomycin) and doxorubicin), antibiotics (e.g., dactinomycin (formerly actinomycin), bleomycin, mithramycin, and anthramycin (AMC)), and anti-mitotic agents (e.g., vincristine, vinblastine, docetaxel, paclitaxel and vinorelbin). Suitable radioisotopes include, but are not limited to, iodine-131, yttrium-90 or indium-111. Further examples of therapeutic moieties are a protein or polypeptide possessing a desired biological activity. Such proteins may include, for example, an enzymatically active toxin, or active fragment thereof, such as abrin, ricin A, pseudomonas exotoxin, or diphtheria toxin; a protein such as tumor necrosis factor or interferon- γ ; or biological response modifiers such as, for example, lymphokines, interleukin-1 (IL-1), interleukin-2 (IL-2), interleukin-6 (IL-6), granulocyte macrophage colony stimulating factor (GM-CSF), granulocyte colony stimulating factor (G-CSF), or other growth factors.

[00140] In some embodiments, the selective binding of the antibody to the complex comprising the non-classical HLA-I (e.g. HLA-E) and the neoantigen induces an immune response. In some embodiments, the immune response comprises activation of T cells. In some embodiments, the T cell is a CD8+ T cell. In some embodiments, the immune response comprises activation of cytotoxic T cells (CTLs).

[00141] In some embodiments, the antibody comprises a light chain (LC) having an amino acid sequence at least about 70% identical to an amino acid sequence set forth as SEQ ID NO: 31. In some embodiments the LC has an amino acid sequence at least about 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 31. In some embodiments, the LC has an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 31.

[00142] In some embodiments, the antibody comprises a heavy chain (HC) having an amino acid sequence at least about 70% identical to an amino acid sequence set forth as SEQ ID NO: 30. In some embodiments the HC has an amino acid sequence at least about 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 30. In some embodiments, the HC has an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 30.

[00143] In some embodiments, the antibody comprises a light chain (LC) having an amino acid sequence at least about 70% identical to an amino acid sequence set forth as SEQ ID NO: 31

and a heavy chain (HC) having an amino acid sequence at least about 70% identical to an amino acid sequence set forth as SEQ ID NO: 30. In some embodiments the LC has an amino acid sequence at least about 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 31 and the HC has an amino acid sequence at least about 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 30. In some embodiments, the LC has an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 31 and the HC has an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 30.

[00144] In some embodiments, the antibody comprises a heavy chain (HC) having an amino acid sequence at least about 70% identical to an amino acid sequence set forth as SEQ ID NO: 32. In some embodiments the HC has an amino acid sequence at least about 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 32. In some embodiments, the HC has an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 32.

[00145] In some embodiments, the antibody comprises a light chain (LC) having an amino acid sequence at least about 70% identical to an amino acid sequence set forth as SEQ ID NO: 31 and a heavy chain (HC) having an amino acid sequence at least about 70% identical to an amino acid sequence set forth as SEQ ID NO: 32. In some embodiments the LC has an amino acid sequence at least about 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 31 and the HC has an amino acid sequence at least about 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 32. In some embodiments, the LC has an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 31 and the HC has an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 32.

[00146] In some embodiments, the antibody comprises a heavy chain (HC) having an amino acid sequence at least about 70% identical to an amino acid sequence set forth as SEQ ID NO: 33. In some embodiments the HC has an amino acid sequence at least about 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 33. In some embodiments, the HC has an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 33.

[00147] In some embodiments, the antibody comprises a light chain (LC) having an amino acid sequence at least about 70% identical to an amino acid sequence set forth as SEQ ID NO: 31 and a heavy chain (HC) having an amino acid sequence at least about 70% identical to an amino acid sequence set forth as SEQ ID NO: 33. In some embodiments the LC has an amino acid sequence at least about 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 31 and the HC has an amino acid sequence at least about 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 33. In some embodiments, the LC has an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 31 and the HC has an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 33.

[00148] In some embodiments, the antibody comprises a light chain (LC) having an amino acid sequence at least about 70% identical to an amino acid sequence set forth as SEQ ID NO: 35. In some embodiments the LC has an amino acid sequence at least about 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 35. In some embodiments, the LC has an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 35.

[00149] In some embodiments, the antibody comprises a heavy chain (HC) having an amino acid sequence at least about 70% identical to an amino acid sequence set forth as SEQ ID NO: 34. In some embodiments the HC has an amino acid sequence at least about 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 34. In some embodiments, the HC has an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 34.

[00150] In some embodiments, the antibody comprises a light chain (LC) having an amino acid sequence at least about 70% identical to an amino acid sequence set forth as SEQ ID NO: 35 and a heavy chain (HC) having an amino acid sequence at least about 70% identical to an amino acid sequence set forth as SEQ ID NO: 34. In some embodiments the LC has an amino acid sequence at least about 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 35 and the HC has an amino acid sequence at least about 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 34. In some embodiments, the LC has an amino acid

sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 35 and the HC has an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 34.

[00151] In some embodiments, the antibody comprises a light chain variable domain (VL) having an amino acid sequence at least about 70% identical to an amino acid sequence set forth as SEQ ID NO: 7. In some embodiments the VL has an amino acid sequence at least about 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 7. In some embodiments, the VL has an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 7.

[00152] In some embodiments, the antibody comprises a heavy chain variable domain (VH) having an amino acid sequence at least about 70% identical to an amino acid sequence set forth as SEQ ID NO: 8. In some embodiments the VH has an amino acid sequence at least about 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 8. In some embodiments, the VH has an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 8.

[00153] In some embodiments, the antibody comprises a light chain variable domain (VL) having an amino acid sequence at least about 70% identical to an amino acid sequence set forth as SEQ ID NO: 7 and a heavy chain variable domain (VH) having an amino acid sequence at least about 70% identical to an amino acid sequence set forth as SEQ ID NO: 8. In some embodiments the VL has an amino acid sequence at least about 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 7 and the VH has an amino acid sequence at least about 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 8. In some embodiments, the VL has an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 7 and the VH has an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 8.

[00154] In some embodiments, the antibody comprises a light chain CDR sequence having an amino acid sequence at least about 70% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 1-3. In some embodiments, the antibody comprises a light chain CDR sequence having an amino acid sequence at least about 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%,

88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 1-3. In some embodiments, the antibody comprises a light chain CDR sequence having an amino acid sequence 100% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 1-3.

[00155] In some embodiments, the antibody comprises a heavy chain CDR sequence having an amino acid sequence at least about 70% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6. In some embodiments, the antibody comprises a heavy chain CDR sequence having an amino acid sequence at least about 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6. In some embodiments, the antibody comprises a heavy chain CDR sequence having an amino acid sequence 100% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6.

[00156] In some embodiments, the antibody comprises a light chain CDR sequence having an amino acid sequence at least about 70% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 1-3 and a heavy chain CDR sequence having an amino acid sequence at least about 70% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6. In some embodiments, the antibody comprises a light chain CDR sequence having an amino acid sequence at least about 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 1-3 and a heavy chain CDR sequence having an amino acid sequence at least about 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6. In some embodiments, the antibody comprises a light chain CDR sequence having an amino acid sequence 100% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 1-3 and a heavy chain CDR sequence having an amino acid sequence at least about 100% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6.

[00157] In some embodiments, the antibody selectively binds to a complex comprising an HLA-E and a neoantigen and comprises at least one of a light chain CDR1 having an amino acid sequence at least about 70% identical to an amino acid sequence set forth as SEQ ID NO: 1, a light chain CDR2 having an amino acid sequence at least about 70% identical to an amino acid sequence set forth as SEQ ID NO: 2, and a light chain CDR3 having an amino acid sequence at least about 70% identical to an amino acid sequence set forth as SEQ ID NO: 3. In some embodiments, the

antibody comprises at least one of a light chain a light chain CDR1 having an amino acid sequence at least about 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 1, a light chain CDR2 having an amino acid sequence at least about 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 2, and a light chain CDR3 having an amino acid sequence at least about 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 3. In some embodiments, the antibody comprises at least one of a light chain CDR1 having an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 1, a light chain CDR2 having an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 2, and a light chain CDR3 having an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 3.

[00158] In some embodiments, the antibody that selectively binds to a complex comprising an HLA-E and a neoantigen comprises at least one of a heavy chain CDR1 having an amino acid sequence at least about 70% identical to an amino acid sequence set forth as SEQ ID NO: 4, a heavy chain CDR2 having an amino acid sequence at least about 70% identical to an amino acid sequence set forth as SEQ ID NO: 5, a heavy chain CDR3 having an amino acid sequence at least about 70% identical to an amino acid sequence set forth as SEQ ID NO: 6. In some embodiments, the antibody comprises at least one of a heavy chain CDR1 having an amino acid sequence at least about 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 4, a heavy chain CDR2 having an amino acid sequence at least about 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 5, a heavy chain CDR3 having an amino acid sequence at least about 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 6. In some embodiments, the antibody comprises at least one of a heavy chain CDR1 having an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 4, a heavy chain CDR2 having an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 5, a heavy chain CDR3 having an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 6.

[00159] In some embodiments, the antibody that selectively bind to a complex comprising an HLA-E and a neoantigen comprises at least one of a light chain CDR1 having an amino acid sequence at least about 70% identical to an amino acid sequence set forth as SEQ ID NO: 1, a light chain CDR2 having an amino acid sequence at least about 70% identical to an amino acid sequence set forth as SEQ ID NO: 2, a light chain CDR3 having an amino acid sequence at least about 70% identical to an amino acid sequence set forth as SEQ ID NO: 3, a heavy chain CDR1 having an amino acid sequence at least about 70% identical to an amino acid sequence set forth as SEQ ID NO: 4, a heavy chain CDR2 having an amino acid sequence at least about 70% identical to an amino acid sequence set forth as SEQ ID NO: 5, and a heavy chain CDR3 having an amino acid sequence at least about 70% identical to an amino acid sequence set forth as SEQ ID NO: 6. In some embodiments, the antibody comprises at least one of a light chain CDR1 having an amino acid sequence at least about 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 1, a light chain CDR2 having an amino acid sequence at least about 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 2, a light chain CDR3 having an amino acid sequence at least about 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 3, a heavy chain CDR1 having an amino acid sequence at least about 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 4, a heavy chain CDR2 having an amino acid sequence at least about 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 5, and a heavy chain CDR3 having an amino acid sequence at least about 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 6. In some embodiments, the antibody comprises at least one of a light chain CDR1 having an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 1, a light chain CDR2 having an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 2, a light chain CDR3 having an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 3, a heavy chain CDR1 having an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 4, a heavy chain CDR2 having an

amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 5, and a heavy chain CDR3 having an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 6.

[00160] In some embodiments, the antibody is a bispecific antibody. In some embodiments, the bispecific the antibody comprises (a) a light chain variable domain (VL) comprising an amino acid sequence at least 70% identical to an amino acid sequence set forth as SEQ ID NO: 7; or a heavy chain variable domain (VH) comprising an amino acid sequence at least 70% identical to an amino acid sequence set forth as SEQ ID NO: 8; and (b) a light chain variable domain (VL) comprising an amino acid sequence at least 70% identical to an amino acid sequence set forth as SEQ ID NO: 15; or a heavy chain variable domain (VH) comprising an amino acid sequence at least 70% identical to an amino acid sequence set forth as SEQ ID NO: 16.

[00161] In some embodiments, the bispecific antibody comprises (a) a light chain variable domain (VL) comprising an amino acid sequence at least 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 7; or a heavy chain variable domain (VH) comprising an amino acid sequence at least 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 8; and (b) a light chain variable domain (VL) comprising an amino acid sequence at least 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 15; or a heavy chain variable domain (VH) comprising an amino acid sequence at least 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 16.

[00162] In some embodiments, the bispecific antibody comprises (a) a light chain variable domain (VL) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 7; or a heavy chain variable domain (VH) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 8; and (b) a light chain variable domain (VL) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 15; or a heavy chain variable domain (VH) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 16.

[00163] In some embodiments, the bispecific antibody comprises (a) a light chain variable domain (VL) comprising an amino acid sequence at least 70% identical to an amino acid sequence

set forth as SEQ ID NO: 7; and a heavy chain variable domain (VH) comprising an amino acid sequence at least 70% identical to an amino acid sequence set forth as SEQ ID NO: 8; and (b) a light chain variable domain (VL) comprising an amino acid sequence at least 70% identical to an amino acid sequence set forth as SEQ ID NO: 15; and a heavy chain variable domain (VH) comprising an amino acid sequence at least 70% identical to an amino acid sequence set forth as SEQ ID NO: 16.

[00164] In some embodiments, the bispecific antibody comprises (a) a light chain variable domain (VL) comprising an amino acid sequence at least 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 7; and a heavy chain variable domain (VH) comprising an amino acid sequence at least 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 8; and (b) a light chain variable domain (VL) comprising an amino acid sequence at least 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 15; and a heavy chain variable domain (VH) comprising an amino acid sequence at least 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 16.

[00165] In some embodiments, the bispecific antibody comprises (a) a light chain variable domain (VL) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 7; and a heavy chain variable domain (VH) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 8; and (b) a light chain variable domain (VL) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 15; and a heavy chain variable domain (VH) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 16.

[00166] In some embodiments, the bispecific antibodies comprise (a) a light chain (LC) comprising an amino acid sequence at least 70% identical to an amino acid sequence set forth as SEQ ID NO:31; or a heavy chain (HC) comprising an amino acid sequence at least 70% identical to an amino acid sequence set forth as SEQ ID NO: 30; and (b) a light chain variable domain (VL) comprising an amino acid sequence at least 70% identical to an amino acid sequence set forth as SEQ ID NO: 15; or a heavy chain variable domain (VH) comprising an amino acid sequence at least 70% identical to an amino acid sequence set forth as SEQ ID NO: 16.

[00167] In some embodiments, the bispecific antibodies comprise (a) a light chain (LC) comprising an amino acid sequence at least 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 31; or a heavy chain (HC) comprising an amino acid sequence at least 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 30; and (b) a light chain variable domain (VL) comprising an amino acid sequence at least 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 15; or a heavy chain variable domain (VH) comprising an amino acid sequence at least 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 16.

[00168] In some embodiments, the bispecific antibodies comprise (a) a light chain (LC) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO:31; or a heavy chain (HC) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 30; and (b) a light chain variable domain (VL) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 15; or a heavy chain variable domain (VH) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 16.

[00169] In some embodiments, the bispecific antibodies comprise (a) a light chain (LC) comprising an amino acid sequence at least 70% identical to an amino acid sequence set forth as SEQ ID NO:31; or a heavy chain (HC) comprising an amino acid sequence at least 70% identical to an amino acid sequence set forth as SEQ ID NO: 32; and (b) a light chain variable domain (VL) comprising an amino acid sequence at least 70% identical to an amino acid sequence set forth as SEQ ID NO: 15; or a heavy chain variable domain (VH) comprising an amino acid sequence at least 70% identical to an amino acid sequence set forth as SEQ ID NO: 16.

[00170] In some embodiments, the bispecific antibodies comprise (a) a light chain (LC) comprising an amino acid sequence at least 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 31; or a heavy chain (HC) comprising an amino acid sequence at least 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 32; and

(b) a light chain variable domain (VL) comprising an amino acid sequence at least 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 15; or a heavy chain variable domain (VH) comprising an amino acid sequence at least 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 16.

[00171] In some embodiments, the bispecific antibodies comprise (a) a light chain (LC) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO:31; or a heavy chain (HC) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 32; and (b) a light chain variable domain (VL) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 15; or a heavy chain variable domain (VH) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 16.

[00172] In some embodiments, the bispecific antibodies comprise (a) a light chain (LC) comprising an amino acid sequence at least 70% identical to an amino acid sequence set forth as SEQ ID NO:31; or a heavy chain (HC) comprising an amino acid sequence at least 70% identical to an amino acid sequence set forth as SEQ ID NO: 33; and (b) a light chain variable domain (VL) comprising an amino acid sequence at least 70% identical to an amino acid sequence set forth as SEQ ID NO: 15; or a heavy chain variable domain (VH) comprising an amino acid sequence at least 70% identical to an amino acid sequence set forth as SEQ ID NO: 16.

[00173] In some embodiments, the bispecific antibodies comprise (a) a light chain (LC) comprising an amino acid sequence at least 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 31; or a heavy chain (HC) comprising an amino acid sequence at least 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 33; and (b) a light chain variable domain (VL) comprising an amino acid sequence at least 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 15; or a heavy chain variable domain (VH) comprising an amino acid sequence at least 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 16.

[00174] In some embodiments, the bispecific antibodies comprise (a) a light chain (LC) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO:31; or a heavy chain (HC) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 33; and (b) a light chain variable domain (VL) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 15; or a heavy chain variable domain (VH) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 16.

[00175] In some embodiments, the bispecific antibodies comprise (a) a light chain (LC) comprising an amino acid sequence at least 70% identical to an amino acid sequence set forth as SEQ ID NO:35; or a heavy chain (HC) comprising an amino acid sequence at least 70% identical to an amino acid sequence set forth as SEQ ID NO: 34; and (b) a light chain variable domain (VL) comprising an amino acid sequence at least 70% identical to an amino acid sequence set forth as SEQ ID NO: 15; or a heavy chain variable domain (VH) comprising an amino acid sequence at least 70% identical to an amino acid sequence set forth as SEQ ID NO: 16.

[00176] In some embodiments, the bispecific antibodies comprise (a) a light chain (LC) comprising an amino acid sequence at least 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 35; or a heavy chain (HC) comprising an amino acid sequence at least 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 34; and (b) a light chain variable domain (VL) comprising an amino acid sequence at least 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 15; or a heavy chain variable domain (VH) comprising an amino acid sequence at least 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 16.

[00177] In some embodiments, the bispecific antibodies comprise (a) a light chain (LC) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO:35; or a heavy chain (HC) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 34; and (b) a light chain variable domain (VL) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 15; or a

heavy chain variable domain (VH) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 16.

[00178] In some embodiments, the bispecific the antibody comprises (a) a light chain complementarity determining region (CDR) having an amino acid sequence at least 70% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 1-3; or a heavy chain complementarity determining region (CDR) having an amino acid sequence at least 70% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6; and (b) a light chain complementarity determining region (CDR) having an amino acid sequence at least 70% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 9-11; or a heavy chain complementarity determining region (CDR) having an amino acid sequence at least 70% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 12-14.

[00179] In some embodiments, the bispecific the antibody comprises (a) a light chain complementarity determining region (CDR) having an amino acid sequence at least 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 1-3; or a heavy chain complementarity determining region (CDR) having an amino acid sequence at least 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6; and (b) a light chain complementarity determining region (CDR) having an amino acid sequence at least 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 9-11; or a heavy chain complementarity determining region (CDR) having an amino acid sequence at least 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 12-14.

[00180] In some embodiments, the bispecific the antibody comprises (a) a light chain complementarity determining region (CDR) having an amino acid sequence 100% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 1-3; or a heavy chain complementarity determining region (CDR) having an amino acid sequence 100% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6; and (b) a light chain complementarity determining region (CDR) having an amino acid sequence 100% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 9-11; or a heavy chain

complementarity determining region (CDR) having an amino acid sequence 100% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 12-14.

[00181] In some embodiments, the bispecific the antibody comprises (a) a light chain complementarity determining region (CDR) having an amino acid sequence at least 70% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 1-3; and a heavy chain complementarity determining region (CDR) having an amino acid sequence at least 70% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6; and (b) a light chain complementarity determining region (CDR) having an amino acid sequence at least 70% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 9-11; and a heavy chain complementarity determining region (CDR) having an amino acid sequence at least 70% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 12-14.

[00182] In some embodiments, the bispecific the antibody comprises (a) a light chain complementarity determining region (CDR) having an amino acid sequence at least 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 1-3; and a heavy chain complementarity determining region (CDR) having an amino acid sequence at least 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6; and (b) a light chain complementarity determining region (CDR) having an amino acid sequence at least 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 9-11; and a heavy chain complementarity determining region (CDR) having an amino acid sequence at least 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 12-14.

[00183] In some embodiments, the bispecific the antibody comprises (a) a light chain complementarity determining region (CDR) having an amino acid sequence 100% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 1-3; and a heavy chain complementarity determining region (CDR) having an amino acid sequence 100% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6; and (b) a light chain complementarity determining region (CDR) having an amino acid sequence 100% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 9-11; and a heavy chain

complementarity determining region (CDR) having an amino acid sequence 100% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 12-14.

[00184] Any suitable route of administration is contemplated for use with the methods disclosed herein. In some embodiments, the antibody is administered by intravenous administration. In some embodiments, the antibody is administered by subcutaneous administration. In some embodiments, the antibody is administered locally. In some embodiments, the antibody is administered systemically (e.g., intravenously, intramuscularly, subcutaneously, intradermally, orally, intranasally, sublingually). In some embodiments, the antibody is formulated as a salve, lotion or emulsion. In some embodiments, the antibody is formulated as a solution. In some embodiments, the antibody is formulated for topical, oral, buccal, or nasal administration.

[00185] In some embodiments, the individual is monitored prior to administration of the antibody. Symptoms are identified and their severity is assessed. An antibody as described herein is administered alone or in combination with additional treatments, singly or multiply over time as discussed herein or known to one of skill in the art. In some embodiments, the individual is monitored such that the efficacy of the treatment regimen is determined. In some embodiments, a treatment regimen is modified in response to preliminary treatment outcomes, such that treatment dose or frequency or dose and frequency is altered so as to attain a desired level of subject response in light of symptom alleviation, side effect reduction, or a combination of symptom alleviation and side effect reduction.

Pharmaceutical Compositions

[00186] Also disclosed herein are pharmaceutical compositions comprising (a) an antibody that selectively bind to a complex comprising a non-classical HLA-I (e.g. HLA-E) and a neoantigen as disclosed herein, and (b) a pharmaceutically acceptable carrier or excipient.

[00187] In some embodiments, the antibody comprises a light chain (LC) having an amino acid sequence at least about 70% identical to an amino acid sequence set forth as SEQ ID NO: 31. In some embodiments the LC has an amino acid sequence at least about 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 31. In some embodiments, the LC has an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 31.

[00188] In some embodiments, the antibody comprises a heavy chain (HC) having an amino acid sequence at least about 70% identical to an amino acid sequence set forth as SEQ ID NO: 30.

In some embodiments the HC has an amino acid sequence at least about 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 30. In some embodiments, the HC has an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 30.

[00189] In some embodiments, the antibody comprises a light chain (LC) having an amino acid sequence at least about 70% identical to an amino acid sequence set forth as SEQ ID NO: 31 and a heavy chain (HC) having an amino acid sequence at least about 70% identical to an amino acid sequence set forth as SEQ ID NO: 30. In some embodiments the LC has an amino acid sequence at least about 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 31 and the HC has an amino acid sequence at least about 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 30. In some embodiments, the LC has an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 31 and the HC has an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 30.

[00190] In some embodiments, the antibody comprises a heavy chain (HC) having an amino acid sequence at least about 70% identical to an amino acid sequence set forth as SEQ ID NO: 32. In some embodiments the HC has an amino acid sequence at least about 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 32. In some embodiments, the HC has an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 32.

[00191] In some embodiments, the antibody comprises a light chain (LC) having an amino acid sequence at least about 70% identical to an amino acid sequence set forth as SEQ ID NO: 31 and a heavy chain (HC) having an amino acid sequence at least about 70% identical to an amino acid sequence set forth as SEQ ID NO: 32. In some embodiments the LC has an amino acid sequence at least about 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 31 and the HC has an amino acid sequence at least about 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 32. In some embodiments, the LC has an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 31 and the HC has an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 32.

[00192] In some embodiments, the antibody comprises a heavy chain (HC) having an amino acid sequence at least about 70% identical to an amino acid sequence set forth as SEQ ID NO: 33. In some embodiments the HC has an amino acid sequence at least about 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 33. In some embodiments, the HC has an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 33.

[00193] In some embodiments, the antibody comprises a light chain (LC) having an amino acid sequence at least about 70% identical to an amino acid sequence set forth as SEQ ID NO: 31 and a heavy chain (HC) having an amino acid sequence at least about 70% identical to an amino acid sequence set forth as SEQ ID NO: 33. In some embodiments the LC has an amino acid sequence at least about 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 31 and the HC has an amino acid sequence at least about 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 33. In some embodiments, the LC has an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 31 and the HC has an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 33.

[00194] In some embodiments, the antibody comprises a light chain (LC) having an amino acid sequence at least about 70% identical to an amino acid sequence set forth as SEQ ID NO: 35. In some embodiments the LC has an amino acid sequence at least about 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 35. In some embodiments, the LC has an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 35.

[00195] In some embodiments, the antibody comprises a heavy chain (HC) having an amino acid sequence at least about 70% identical to an amino acid sequence set forth as SEQ ID NO: 34. In some embodiments the HC has an amino acid sequence at least about 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 34. In some embodiments, the HC has an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 34.

[00196] In some embodiments, the antibody comprises a light chain (LC) having an amino acid sequence at least about 70% identical to an amino acid sequence set forth as SEQ ID NO: 35 and a heavy chain (HC) having an amino acid sequence at least about 70% identical to an amino acid

sequence set forth as SEQ ID NO: 34. In some embodiments the LC has an amino acid sequence at least about 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 35 and the HC has an amino acid sequence at least about 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 34. In some embodiments, the LC has an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 35 and the HC has an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 34.

[00197] In some embodiments, the antibody comprises a light chain variable domain (VL) having an amino acid sequence at least about 70% identical to an amino acid sequence set forth as SEQ ID NO: 7. In some embodiments, the VL has an amino acid sequence at least about 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 7. In some embodiments, the VL has an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 7.

[00198] In some embodiments, the antibody comprises a heavy chain variable domain (VH) having an amino acid sequence at least about 70% identical to an amino acid sequence set forth as SEQ ID NO: 8. In some embodiments, the VH has an amino acid sequence at least about 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 8. In some embodiments, the VH has an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 8.

[00199] In some embodiments, the antibody comprises a light chain variable domain (VL) having an amino acid sequence at least about 70% identical to an amino acid sequence set forth as SEQ ID NO: 7 and a heavy chain variable domain (VH) having an amino acid sequence at least about 70% identical to an amino acid sequence set forth as SEQ ID NO: 8. In some embodiments, the VL has an amino acid sequence at least about 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 7 and the VH has an amino acid sequence at least about 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 8. In some embodiments, the VL has an amino acid sequence 100% identical to an amino acid sequence set

forth as SEQ ID NO: 7 and the VH has an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 8.

[00200] In some embodiments, the antibody comprises a light chain CDR sequence having an amino acid sequence at least about 70% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 1-3. In some embodiments, the antibody comprises a light chain CDR sequence having an amino acid sequence at least about 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 1-3. In some embodiments, the antibody comprises a light chain CDR sequence having an amino acid sequence 100% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 1-3.

[00201] In some embodiments, the antibody comprises a heavy chain CDR sequence having an amino acid sequence at least about 70% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6. In some embodiments, the antibody comprises a heavy chain CDR sequence having an amino acid sequence at least about 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6. In some embodiments, the antibody comprises a heavy chain CDR sequence having an amino acid sequence 100% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6.

[00202] In some embodiments, the antibody comprises a light chain CDR sequence having an amino acid sequence at least about 70% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 1-3 and a heavy chain CDR sequence having an amino acid sequence at least about 70% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6. In some embodiments, the antibody comprises a light chain CDR sequence having an amino acid sequence at least about 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 1-3 and a heavy chain CDR sequence having an amino acid sequence at least about 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6. In some embodiments, the antibody comprises a light chain CDR sequence having an amino acid sequence 100% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 1-3 and a heavy chain CDR sequence having an amino acid sequence at least about 100% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6.

[00203] In some embodiments, the antibody that selectively binds to a complex comprising an HLA-E and a neoantigen comprises at least one of a light chain CDR1 having an amino acid sequence at least about 70% identical to an amino acid sequence set forth as SEQ ID NO: 1, a light chain CDR2 having an amino acid sequence at least about 70% identical to an amino acid sequence set forth as SEQ ID NO: 2, and a light chain CDR3 having an amino acid sequence at least about 70% identical to an amino acid sequence set forth as SEQ ID NO: 3. In some embodiments, the antibody comprises at least one of a light chain a light chain CDR1 having an amino acid sequence at least about 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 1, a light chain CDR2 having an amino acid sequence at least about 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 2, and a light chain CDR3 having an amino acid sequence at least about 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 3. In some embodiments, the antibody comprises at least one of a light chain CDR1 having an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 1, a light chain CDR2 having an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 2, and a light chain CDR3 having an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 3.

[00204] In some embodiments, the antibody that selectively bind to a complex comprising an HLA-E and a neoantigen comprises at least one of a heavy chain CDR1 having an amino acid sequence at least about 70% identical to an amino acid sequence set forth as SEQ ID NO: 4, a heavy chain CDR2 having an amino acid sequence at least about 70% identical to an amino acid sequence set forth as SEQ ID NO: 5, a heavy chain CDR3 having an amino acid sequence at least about 70% identical to an amino acid sequence set forth as SEQ ID NO: 6. In some embodiments, the antibody comprises at least one of a heavy chain CDR1 having an amino acid sequence at least about 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 4, a heavy chain CDR2 having an amino acid sequence at least about 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 5, a heavy chain CDR3 having an amino acid sequence at least about 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%,

94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 6. In some embodiments, the antibody comprises at least one of a heavy chain CDR1 having an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 4, a heavy chain CDR2 having an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 5, a heavy chain CDR3 having an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 6.

[00205] In some embodiments, the antibody that selectively bind to a complex comprising an HLA-E and a neoantigen comprises at least one of a light chain CDR1 having an amino acid sequence at least about 70% identical to an amino acid sequence set forth as SEQ ID NO: 1, a light chain CDR2 having an amino acid sequence at least about 70% identical to an amino acid sequence set forth as SEQ ID NO: 2, a light chain CDR3 having an amino acid sequence at least about 70% identical to an amino acid sequence set forth as SEQ ID NO: 3, a heavy chain CDR1 having an amino acid sequence at least about 70% identical to an amino acid sequence set forth as SEQ ID NO: 4, a heavy chain CDR2 having an amino acid sequence at least about 70% identical to an amino acid sequence set forth as SEQ ID NO: 5, and a heavy chain CDR3 having an amino acid sequence at least about 70% identical to an amino acid sequence set forth as SEQ ID NO: 6. In some embodiments, the antibody comprises at least one of a light chain CDR1 having an amino acid sequence at least about 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 1, a light chain CDR2 having an amino acid sequence at least about 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 2, a light chain CDR3 having an amino acid sequence at least about 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 3, a heavy chain CDR1 having an amino acid sequence at least about 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 4, a heavy chain CDR2 having an amino acid sequence at least about 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 5, and a heavy chain CDR3 having an amino acid sequence at least about 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 6.

In some embodiments, the antibody comprises at least one of a light chain CDR1 having an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 1, a light chain CDR2 having an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 2, a light chain CDR3 having an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 3, a heavy chain CDR1 having an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 4, a heavy chain CDR2 having an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 5, and a heavy chain CDR3 having an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 6.

[00206] In some embodiments, the antibody is a bispecific antibody. In some embodiments, the bispecific the antibody comprises (a) a light chain variable domain (VL) comprising an amino acid sequence at least 70% identical to an amino acid sequence set forth as SEQ ID NO: 7; or a heavy chain variable domain (VH) comprising an amino acid sequence at least 70% identical to an amino acid sequence set forth as SEQ ID NO: 8; and (b) a light chain variable domain (VL) comprising an amino acid sequence at least 70% identical to an amino acid sequence set forth as SEQ ID NO: 15; or a heavy chain variable domain (VH) comprising an amino acid sequence at least 70% identical to an amino acid sequence set forth as SEQ ID NO: 16.

[00207] In some embodiments, the bispecific antibody comprises (a) a light chain variable domain (VL) comprising an amino acid sequence at least 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 7; or a heavy chain variable domain (VH) comprising an amino acid sequence at least 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 8; and (b) a light chain variable domain (VL) comprising an amino acid sequence at least 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 15; or a heavy chain variable domain (VH) comprising an amino acid sequence at least 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 16.

[00208] In some embodiments, the bispecific antibody comprises (a) a light chain variable domain (VL) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 7; or a heavy chain variable domain (VH) comprising an amino acid sequence 100%

identical to an amino acid sequence set forth as SEQ ID NO: 8; and (b) a light chain variable domain (VL) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 15; or a heavy chain variable domain (VH) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 16.

[00209] In some embodiments, the bispecific antibody comprises (a) a light chain variable domain (VL) comprising an amino acid sequence at least 70% identical to an amino acid sequence set forth as SEQ ID NO: 7; and a heavy chain variable domain (VH) comprising an amino acid sequence at least 70% identical to an amino acid sequence set forth as SEQ ID NO: 8; and (b) a light chain variable domain (VL) comprising an amino acid sequence at least 70% identical to an amino acid sequence set forth as SEQ ID NO: 15; and a heavy chain variable domain (VH) comprising an amino acid sequence at least 70% identical to an amino acid sequence set forth as SEQ ID NO: 16.

[00210] In some embodiments, the bispecific antibody comprises (a) a light chain variable domain (VL) comprising an amino acid sequence at least 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 7; and a heavy chain variable domain (VH) comprising an amino acid sequence at least 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 8; and (b) a light chain variable domain (VL) comprising an amino acid sequence at least 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 15; and a heavy chain variable domain (VH) comprising an amino acid sequence at least 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 16.

[00211] In some embodiments, the bispecific antibody comprises (a) a light chain variable domain (VL) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 7; and a heavy chain variable domain (VH) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 8; and (b) a light chain variable domain (VL) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 15; and a heavy chain variable domain (VH) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 16.

[00212] In some embodiments, the bispecific antibodies comprise (a) a light chain (LC) comprising an amino acid sequence at least 70% identical to an amino acid sequence set forth as

SEQ ID NO:31; or a heavy chain (HC) comprising an amino acid sequence at least 70% identical to an amino acid sequence set forth as SEQ ID NO: 30; and (b) a light chain variable domain (VL) comprising an amino acid sequence at least 70% identical to an amino acid sequence set forth as SEQ ID NO: 15; or a heavy chain variable domain (VH) comprising an amino acid sequence at least 70% identical to an amino acid sequence set forth as SEQ ID NO: 16.

[00213] In some embodiments, the bispecific antibodies comprise (a) a light chain (LC) comprising an amino acid sequence at least 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 31; or a heavy chain (HC) comprising an amino acid sequence at least 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 30; and (b) a light chain variable domain (VL) comprising an amino acid sequence at least 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 15; or a heavy chain variable domain (VH) comprising an amino acid sequence at least 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 16.

[00214] In some embodiments, the bispecific antibodies comprise (a) a light chain (LC) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO:31; or a heavy chain (HC) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 30; and (b) a light chain variable domain (VL) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 15; or a heavy chain variable domain (VH) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 16.

[00215] In some embodiments, the bispecific antibodies comprise (a) a light chain (LC) comprising an amino acid sequence at least 70% identical to an amino acid sequence set forth as SEQ ID NO:31; or a heavy chain (HC) comprising an amino acid sequence at least 70% identical to an amino acid sequence set forth as SEQ ID NO: 32; and (b) a light chain variable domain (VL) comprising an amino acid sequence at least 70% identical to an amino acid sequence set forth as SEQ ID NO: 15; or a heavy chain variable domain (VH) comprising an amino acid sequence at least 70% identical to an amino acid sequence set forth as SEQ ID NO: 16.

[00216] In some embodiments, the bispecific antibodies comprise (a) a light chain (LC) comprising an amino acid sequence at least 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 31; or a heavy chain (HC) comprising an amino acid sequence at least 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 32; and (b) a light chain variable domain (VL) comprising an amino acid sequence at least 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 15; or a heavy chain variable domain (VH) comprising an amino acid sequence at least 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 16.

[00217] In some embodiments, the bispecific antibodies comprise (a) a light chain (LC) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO:31; or a heavy chain (HC) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 32; and (b) a light chain variable domain (VL) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 15; or a heavy chain variable domain (VH) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 16.

[00218] In some embodiments, the bispecific antibodies comprise (a) a light chain (LC) comprising an amino acid sequence at least 70% identical to an amino acid sequence set forth as SEQ ID NO:31; or a heavy chain (HC) comprising an amino acid sequence at least 70% identical to an amino acid sequence set forth as SEQ ID NO: 33; and (b) a light chain variable domain (VL) comprising an amino acid sequence at least 70% identical to an amino acid sequence set forth as SEQ ID NO: 15; or a heavy chain variable domain (VH) comprising an amino acid sequence at least 70% identical to an amino acid sequence set forth as SEQ ID NO: 16.

[00219] In some embodiments, the bispecific antibodies comprise (a) a light chain (LC) comprising an amino acid sequence at least 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 31; or a heavy chain (HC) comprising an amino acid sequence at least 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 33; and

(b) a light chain variable domain (VL) comprising an amino acid sequence at least 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 15; or a heavy chain variable domain (VH) comprising an amino acid sequence at least 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 16.

[00220] In some embodiments, the bispecific antibodies comprise (a) a light chain (LC) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO:31; or a heavy chain (HC) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 33; and (b) a light chain variable domain (VL) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 15; or a heavy chain variable domain (VH) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 16

[00221] In some embodiments, the bispecific antibodies comprise (a) a light chain (LC) comprising an amino acid sequence at least 70% identical to an amino acid sequence set forth as SEQ ID NO:35; or a heavy chain (HC) comprising an amino acid sequence at least 70% identical to an amino acid sequence set forth as SEQ ID NO: 34; and (b) a light chain variable domain (VL) comprising an amino acid sequence at least 70% identical to an amino acid sequence set forth as SEQ ID NO: 15; or a heavy chain variable domain (VH) comprising an amino acid sequence at least 70% identical to an amino acid sequence set forth as SEQ ID NO: 16.

[00222] In some embodiments, the bispecific antibodies comprise (a) a light chain (LC) comprising an amino acid sequence at least 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 35; or a heavy chain (HC) comprising an amino acid sequence at least 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 34; and (b) a light chain variable domain (VL) comprising an amino acid sequence at least 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 15; or a heavy chain variable domain (VH) comprising an amino acid sequence at least 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence set forth as SEQ ID NO: 16.

[00223] In some embodiments, the bispecific antibodies comprise (a) a light chain (LC) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO:35; or a heavy chain (HC) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 34; and (b) a light chain variable domain (VL) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 15; or a heavy chain variable domain (VH) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 16.

[00224] In some embodiments, the bispecific the antibody comprises (a) a light chain complementarity determining region (CDR) having an amino acid sequence at least 70% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 1-3; or a heavy chain complementarity determining region (CDR) having an amino acid sequence at least 70% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6; and (b) a light chain complementarity determining region (CDR) having an amino acid sequence at least 70% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 9-11; or a heavy chain complementarity determining region (CDR) having an amino acid sequence at least 70% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 12-14.

[00225] In some embodiments, the bispecific the antibody comprises (a) a light chain complementarity determining region (CDR) having an amino acid sequence at least 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 1-3; or a heavy chain complementarity determining region (CDR) having an amino acid sequence at least 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6; and (b) a light chain complementarity determining region (CDR) having an amino acid sequence at least 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 9-11; or a heavy chain complementarity determining region (CDR) having an amino acid sequence at least 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 12-14.

[00226] In some embodiments, the bispecific the antibody comprises (a) a light chain complementarity determining region (CDR) having an amino acid sequence 100% identical to at

least one of the amino acid sequences set forth as SEQ ID NOS: 1-3; or a heavy chain complementarity determining region (CDR) having an amino acid sequence 100% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6; and (b) a light chain complementarity determining region (CDR) having an amino acid sequence 100% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 9-11; or a heavy chain complementarity determining region (CDR) having an amino acid sequence 100% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 12-14.

[00227] In some embodiments, the the antibody comprises comprise (a) a light chain complementarity determining region (CDR) having an amino acid sequence at least 70% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 1-3; and a heavy chain complementarity determining region (CDR) having an amino acid sequence at least 70% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6; and (b) a light chain complementarity determining region (CDR) having an amino acid sequence at least 70% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 9-11; and a heavy chain complementarity determining region (CDR) having an amino acid sequence at least 70% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 12-14.

[00228] In some embodiments, the bispecific antibody comprises (a) a light chain complementarity determining region (CDR) having an amino acid sequence at least 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 1-3; and a heavy chain complementarity determining region (CDR) having an amino acid sequence at least 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6; and (b) a light chain complementarity determining region (CDR) having an amino acid sequence at least 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 9-11; and a heavy chain complementarity determining region (CDR) having an amino acid sequence at least 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 12-14.

[00229] In some embodiments, the bispecific antibody comprises (a) a light chain complementarity determining region (CDR) having an amino acid sequence 100% identical to at

least one of the amino acid sequences set forth as SEQ ID NOS: 1-3; and a heavy chain complementarity determining region (CDR) having an amino acid sequence 100% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6; and (b) a light chain complementarity determining region (CDR) having an amino acid sequence 100% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 9-11; and a heavy chain complementarity determining region (CDR) having an amino acid sequence 100% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 12-14.

[00230] In some embodiments, excipients for use with the compositions disclosed herein include maleic acid, tartaric acid, lactic acid, citric acid, acetic acid, sodium bicarbonate, sodium phosphate, histidine, glycine, sodium chloride, potassium chloride, calcium chloride, zinc chloride, water, dextrose, N-methylpyrrolidone, dimethyl sulfoxide, N,N-dimethylacetamide, ethanol, propylene glycol, polyethylene glycol, diethylene glycol monoethyl ether, and surfactant polyoxyethylene-sorbitan monooleate.

[00231] In some embodiments, the compositions further comprise an additional therapeutic agent. In some embodiments, the therapeutic agent is a chemotherapeutic agent. The chemotherapeutic agents can include, among others, cytotoxic agents, anti-metabolite agents (e.g., folate antagonists, purine analogs, pyrimidine analogs, etc.), topoisomerase inhibitors (e.g., camptothecin derivatives, anthracenedione, anthracyclines, epipodophyllotoxins, quinoline alkaloids, etc.), anti-microtubule agents (e.g., taxanes, vinca alkaloids), protein synthesis inhibitors (e.g., cephalotaxine, camptothecin derivatives, quinoline alkaloids), alkylating agents (e.g., alkyl sulfonates, ethylenimines, nitrogen mustards, nitrosoureas, platinum derivatives, triazenes, etc.), alkaloids, terpenoids, and kinase inhibitors.

[00232] In some embodiments, the antibody and the therapeutic agent are in the same formulation. In some embodiments, the antibody and the therapeutic agent are in different formulation. In some embodiments, antibody described herein is used prior to the administration of the other therapeutic agent. In some embodiments, antibody described herein is used concurrently with the administration of the other therapeutic agent. In some embodiments, antibody described herein is used subsequent to the administration of the other therapeutic agent.

[00233] Pharmaceutical formulations are made to be compatible with a particular local, regional or systemic administration or delivery route. Thus, pharmaceutical formulations include carriers, diluents, or excipients suitable for administration by particular routes. Specific non-limiting examples of routes of administration for compositions herein are parenteral, e.g., intravenous, intra-

arterial, intradermal, intramuscular, subcutaneous, intra-pleural, transdermal (topical), transmucosal, intra-cranial, intra-spinal, intra-ocular, rectal, oral (alimentary), mucosal administration, and any other formulation suitable for the treatment method or administration protocol.

[00234] Solutions or suspensions used for parenteral application include: a sterile diluent such as water for injection, saline solution, fixed oils, polyethylene glycols, glycerine, propylene glycol or other synthetic solvents; antibacterial agents such as benzyl alcohol or methyl parabens; antioxidants such as ascorbic acid or sodium bisulfate; chelating agents such as ethylenediaminetetraacetic acid; buffers such as acetates, citrates or phosphates; and agents for the adjustment of tonicity such as sodium chloride or dextrose. In some embodiments, pH is adjusted with acids or bases, such as hydrochloric acid or sodium hydroxide.

[00235] Pharmaceutical formulations for injection include sterile aqueous solutions (where water soluble) or dispersions and sterile powders for the extemporaneous preparation of sterile injectable solutions or dispersion. For intravenous administration, suitable carriers include physiological saline, bacteriostatic water, Cremophor EL™ (BASF, Parsippany, N.J.), or phosphate buffered saline (PBS). In some embodiments, the carrier is a solvent or dispersion medium containing, for example, water, ethanol, polyol (for example, glycerol, propylene glycol, and liquid polyethylene glycol, and the like), or suitable mixtures thereof. Fluidity is maintained, in some embodiments, for example, by the use of a coating such as lecithin, by the maintenance of the required particle size in the case of dispersion, and by the use of surfactants. Antibacterial and antifungal agents include, for example, parabens, chlorobutanol, phenol, ascorbic acid, and thimerosal. Isotonic agents, for example, sugars; polyalcohols such as mannitol or sorbitol; or sodium chloride, in some embodiments, are included in the composition. In some cases, also included is an agent which delays absorption, for example, aluminum monostearate or gelatin prolongs absorption of injectable compositions.

[00236] Sterile injectable formulations are prepared by incorporating the active composition in the required amount in an appropriate solvent with one or a combination of above ingredients. Generally, dispersions are prepared by incorporating the active composition into a sterile vehicle containing a basic dispersion medium and any other ingredient. In the case of sterile powders for the preparation of sterile injectable solutions, methods of preparation include, for example, vacuum drying and freeze-drying which yields a powder of the active ingredient plus any additional desired ingredient from a previously prepared solution thereof.

[00237] For transmucosal or transdermal administration, penetrants appropriate to the barrier to be permeated are used in the formulation. Such penetrants are known in the art, and include, for example, for transmucosal administration, detergents, bile salts, and fusidic acid derivatives. In some embodiments, transmucosal administration is accomplished through the use of nasal sprays, inhalation devices (e.g., aspirators) or suppositories. For transdermal administration, the active compounds are formulated into ointments, salves, gels, creams or patches.

[00238] In some embodiments, the pharmaceutical formulations are prepared with carriers that protect against rapid elimination from the body, such as a controlled release formulation or a time delay material such as glyceryl monostearate or glyceryl stearate. The formulations, in some embodiments, are also delivered using articles of manufacture such as implants and microencapsulated delivery systems to achieve local, regional or systemic delivery or controlled or sustained release.

EXAMPLES

[00239] The following examples are given for the purpose of illustrating various embodiments of the invention and are not meant to limit the present invention in any fashion. The present examples, along with the methods described herein are presently representative of preferred embodiments, are exemplary, and are not intended as limitations on the scope of the invention. Changes therein and other uses which are encompassed within the spirit of the invention as defined by the scope of the claims will occur to those skilled in the art.

Example 1. Generation of antibodies

[00240] R4 clone was first isolated from a semi-synthetic human antibody phage library. In brief, this was performed as follows. A human scFv antibody phage display library (1.42×10^9 clones) constructed by Creative Biolabs (HuScL-2 phage library) was used to screen against HLA-G signal peptide/HLA-E*0103 complex (ABI-V-0025; VMAPRTLFL). Briefly, 30 μ g of a mix of five internal peptide/HLA-A2*0201 complexes (ABI-AV-007-Biot, ABI-AV-0010-Biot, ABI-AV-0014-Biot, ABI-AV-0019 and ABI-AB-0030-Biot) were used for depletion and pre-blocking, followed by enrichment with 50 μ g of ABI-V-0025. The enrichment factor of the phage library was 2.73×10^6 (phage input: 5×10^{11} , phage output: 1.83×10^5). This process was repeated for the second round of biopanning, with an enrichment factor of 4.03×10^2 . This process was repeated for the third round of biopanning, but using 20 μ g of the complex mix for depletion (enrichment factor 2.31×10^2). For the fourth round of biopanning, 50 μ g of ABI-V-0018 was used for depletion and pre-blocking, followed by enrichment with 50 μ g of ABI-V-0025 (enrichment factor 44). From the phage output of the fourth round of biopanning, 40 clones were picked and sequenced, revealing one unique sequence. This clone was designated as R4 (clone 1) (**Fig. 1A-Fig. 1B**). To determine affinity of the R4 antibody it was diluted in 0.1% BSA, 0.1% Tween20, PBS dilution/wash buffer and immobilized on the ForteBio Octet Protein A biosensor tip at 20 μ g/ml for 50 seconds. Tips were subsequently washed in dilution/wash buffer for 50 seconds. Antibody binding association was measured using six concentrations (serial dilutions starting at 100 μ g/ml in dilution/wash buffer) of canonical 0025-E 01:03 monomer complex over the course of 150 seconds immediately followed by dissociation (dilution/wash buffer) for 150 seconds (**Fig. 1C**). The equilibrium dissociation constant (KD) for clone R4 (clone 1) was determined to be 411 nM (**Fig. 1D**).

[00241] *Affinity maturation of R4: Cycle 2:* To increase the binding affinity of clone R4 to V-0025, the R4 scFv construct was cloned into a yeast vector to create a library of R4 mutants by

changing two amino acid in the CDRH3 region. In brief, the yeast display library generated used EBY100 yeast competent cells that were prepared for transformation by incubation in 100 mM lithium acetate (LiAc, Sigma) plus 10 mM Dithiothreitol (DTT, Sigma). Electroporation was achieved using a GenePulser (BioRad) with 60 OD prepared yeast per 2 mm cuvette (BioRad) in 10 mM LiAc, with 1 µg of scFv clones and 100 ng of pYES3 (ThermoFisher) altered to include Aga2 after the GAL1 promoter and a Flag (DYKDDDDK) epitope tag after the scFv. To determine the number of transformants, 100 µL of 1/10, 1/100 and 1/1000 dilutions of transformed yeast were spread on glucose plates minus tryptophan and uracil (D-UT, Teknova). Transformation efficiency was calculated after incubation at 30°C for 2 days. Random clones were then picked for insertion diversity by PCR. Yeast were grown at 30°C with shaking at 200 rpm in CM broth with glucose minus tryptophan and uracil (D-UT, Teknova). scFv surface induction was achieved by growing yeast for at least 20 hrs in CM broth with galactose minus tryptophan and uracil (G-UT, Teknova) supplemented with 0.1% raffinose (Sigma) (GR-UT).

[00242] Yeast were stained after first blocking with 2% BSA in PBS 0.05% tween (blocking buffer) for 30 minutes to 1 hour at room temperature with rotation. Yeast were then incubated with biotinylated peptide/HLA complex monomers on ice for 30 minutes to 90 minutes, depending on monomer concentration. Secondary labeling was achieved with Streptavidin PE (ThermoFisher) and DYKDDDDK epitope tag Alexa Fluor 488 (R&D Systems) on ice for 30 minutes. Samples were acquired using a LSR II flow cytometer (BD Biosciences) or a CytoFLEX S (Beckman Coulter). Data was prepared using FlowJo Software version 10 or FACSDiva (BD Biosciences).

[00243] Screening was achieved by either magnetic-activated cell sorting (MACS) or fluorescence-activated cell sorting (FACS), using at least ten-fold coverage of the library size. For MACS screening, yeast were first blocked with 2% BSA in PBS 0.05% tween (blocking buffer) for 30 minutes to 1 hour at room temperature with rotation. Biotinylated peptide/HLA complex monomers were then incubated on ice for 30 minutes at 1 µM. Secondary labeling was achieved using streptavidin microbeads (Miltenyi Biotec). Labeled yeast were poured over a MACS Column on a MACS Separator (Miltenyi Biotec). Yeast bound to the column were harvested and considered as an enriched population. For FACS screening, yeast were prepared as described in the flow cytometry section. Samples were sorted using a FACS Aria II (BD Bioscience). Sorted yeast were considered an enriched population.

[00244] Unique scFv clones were identified by plating. After two days at 30°C, individual colonies were picked and analyzed by PCR. Full-length human IgG1 of the selected clones were

produced in Expi293F (ThermoFisher) cells. Briefly, antibody variable regions were subcloned into mammalian expression vectors, with matching human kappa light-chain constant region (pFUSE2ss-CLlg-hK, Invivogen) and human IgG1 constant region (pFUSEss-CHlg-hG1, Invivogen) sequences. Vectors were transfected at a 2:3 light chain:heavy chain ratio. Antibodies were purified with protein A resin (Genscript) and confirmed in reducing and non-reducing conditions by electrophoresis.

[00245] The first round of selection was performed using 1 μ M of V-0025. Gating was based on binding by the parent (R4); parent exhibited 0.11% to V-0025 while the cycle 2 library exhibited 1.66%, indicating the presence of higher affinity binders (**Fig. 2A**). Round two sort used 100nM V-0025. The cycle 2 library showed 0.23% binding while the parent showed 0%; no binding was observed to a negative control (V-0018) (**Fig. 2B**). The third round of sorting used 10nM V-0025, with 1.05% binding observed (**Fig. 2C**). The final round of sorting incorporated a Koff; briefly, V-0025 was incubated for 30 minutes at 100nM, followed by incubation with R4 in full-length hIgG1 format (R4-IgG1). R4-IgG1 was added at 500nM for various time points to act as an antibody sink. Thus, a final round of sorting was done using Koff pressure to select for top clones (**Fig. 2D**). To identify unique clones, individual colonies were picked and sequenced (n=48). Ten unique clones were identified (**Table 2**) and binding affinity was compared with the parent clone. Of the unique clones, six clones were shown to have at least 100-fold greater binding to V-0025 compared with the parent (**Fig. 3A-Fig. 3D**). One clone (clone R2A_1), in addition to having increased binding affinity, also exhibited superior selectivity and was selected for additional analysis (**Fig. 3E-Fig. 3G**).

Table 2. Unique clones and sequence modifications

Index	Name	CDRH3
1	parent	XXXXXXXX
2	R2A_1	XLXNXXX
3	R2A_3	XHXTXXX
4	R2A_8	XHXAXXX
5	R2B_1	XHXNXXX
6	R2B_3	XHXRXXX
7	R2B_8	XHXWXXX
8	oR2A_1	XYXTXXX
9	oR2A_2	XVXXXXX
10	oR2A_3	XLXSXXX
11	R3A2	XHXVXXX

[00246] *Characterization of clone R2A_1*: Clone R2A_1 was converted from scFv to full-length hIgG1 for testing by ELISA and for cell staining. Based on ELISA data, affinity was measured at about 20nM (data not shown), which represents over 10-fold increase in affinity compared with the parent clone, R4. To check antibody stability, binding was compared after storing the antibody at 37°C for 72hr. As shown in **Fig. 4** binding by R2A_1 to A549-B4 cells was heavily compromised when the antibody had been stored at 37°C for 72hr.

[00247] *Stabilization of clone R2A_1*: In order to increase the stability of R2A_1, several alterations were made to amino acids in the framework regions of both VH and VL. For the VL, the CDRL2 was modified to match its germline (IGKV1-39). This also removed an N-linked glycosylation site. For the VH, in framework region 1, Gln5 was changed to match germline (Leu5). Also in framework region 1, Met18 was changed to match germline (Leu18). The stabilized clone was referred to as R4c1 H1-L1. The scFv sequence was inserted into yeast for display and compared with the parent (R2A_1). While there was some loss in affinity, there was no alteration in specificity (data not shown).

[00248] To generate an antibody with greater affinity and broader specificity, a yeast display library was generated based off of R4c1-H1-L1 and introduced four amino acid mutations in the CDRL3 region, meaning that 44% of the CDRL3 sequence could potentially be altered from the parent. As shown in **Fig. 5A** (R0), very few clones exhibited binding to target, although there were a select group that had greater binding to target than parent. A sort was done (R1 out) using target at 10nM with gating made to only select clones with greater binding affinity than the parent (**Fig. 6A**). The R1 library was checked for binding to target, and a substantial increase was observed in the number of clones binding with improved affinity compared with parent (**Fig. 5A**, R1). To select for clones with enhanced affinity, the R1 library was subjected to Koff pressure. Briefly, the library was incubated with 10nM of target. After washing, 1µM of the parent clone as a full length IgG1 was added for 15 to 120 minutes to act as an antibody sink. Any yeast still showing binding to target indicate a greater Koff compared with the parent clone. As shown in **Fig. 5B**, yeast clones were observed that maintained binding with target even after 120 minutes in the antibody sink. To select for these highly improved clones, a final sort (R2 out) was done using Koff with target at 10nM and parent clone-IgG1 at 1µM for 45 minutes as the antibody sink, with sort gate made to collect only the clones with the highest affinity (**Fig 6B**). After sorting, individual clones were isolated and sequenced (n=60). 21 unique clones were found (**Table 3**) and were checked for binding to target at

1 and 0.1 nM (Fig. 7). The three with the top binding to target were selected for additional testing (clone R2-A01, R2-A12, R2-C09, Fig. 7 black arrows).

Table 3. Unique clones

Clone	CDRL3
Parent	XXXXXXXXXX
R2-B08	GXXXXXWKM
R2-A03	GXXXXXWLM
R2-C03	GXXXXXWRM
R2-A08	XNXXXXHDV
R2-A01	XNXXXXWEX
R2-A04	XNXXXXWVA
R2-C08	XNXXXXWVV
R2-B07	XXXXCXFRP
R2-A05	XXXXCXXSL
R2-A07	XXXXNXWMP
R2-A10	XXXXSXHTP
R2-A11	XXXXSXWEG
R2-B06	XXXXSXYDV
R2-C04	XXXXXXFTP
R2-B03	XXXXXXWFP
R2-A06	XXXXXXWKC
R2-C02	XXXXXXWWP
R2-C05	XXXXXXYKP
R2-A12	XXSXXXWDM
R2-C09	XNXXXXWEA
R2-D05	XXTXXXFTM

Example 2. Characterization of top clones by ELISA, FACS and label-free technology

[00249] The top three clones identified from yeast display were made as hIgG1 and tested for specificity and affinity. Of the three clones tested, R2-A12 exhibited the best affinity and the broadest specificity (data not shown). R2-A12 was given the designation ABX0020 and produced in CHO cells using a 1-L transient transfection protocol followed by purification by Protein-A affinity chromatography. Sample purity was determined by SDS-PAGE reduced (two bands representing heavy and light chains) and non-reduced (single band at ~150kD) (Fig. 8A) and by observing a single peak by size exclusion chromatography (Fig. 8B). ABX0020 was first tested against a broad array of peptide/HLA complexes. As shown in Fig. 9A, HLA-E clone 3D12 binds to all HLA-E complexes, including peptide-empty HLA-E. However, ABX0020 was specific for classical HLA

signal peptide/HLA-E complexes (**Fig. 9B**). It also recognized the non-classical HLA, HLA-G signal peptide/HLA-E complex. It did not recognize any additional peptide/HLA-E complexes, or any peptide/HLA-A2 complexes. No cross-reactivity was observed with the mouse homologue of HLA-E (Qa1b). For the ELISA, highly pure HLA-E 01:03 and HLA-A2 02:01 monomer complexes (diluted in 0.1% BSA, 0.1% Tween20, PBS dilution/wash buffer) was immobilized on neutravidin coated microarray plate at 0.25 µg/ml for one hour at RT. The plate was subsequently washed in dilution/wash buffer 5X. Antibodies diluted to 1 µg/ml in dilution/wash buffer were incubated for one hour at RT and plate was subsequently washed in dilution/wash buffer 5X. Anti-mouse and anti-human HRP conjugate was diluted 1:5000 in dilution/wash buffer and incubated for 30 minutes at RT then subsequently washed 5X in dilution/wash buffer. TMB substrate was added to plate wells and incubated for 15 minutes at 50 ul/well. 1N HCl stop solution was added at 50 ul/well before reading plate at 450 nm absorbance.

[00250] To determine whether ABX0020 recognized classical HLA I signal peptide presented by two different phenotypes of HLA-E, namely HLA-E 01:03 and HLA-E 01:01, monomer complexes of each were used in an ELISA as described above. No difference was observed between binding to the peptides in the two HLA-E alleles; HLA-E*0101 and *0103 (**Fig. 10A-Fig. 10B**).

[00251] *Affinity determination for ABX0020:* The binding affinity of ABX0020 was determined using label-free technology (Resonant Sensors, Inc., ResoSens instrument). The dissociation equilibrium constant (KD) was found to be 1.87nM or an improvement of more than 200-fold over the R4 clone (**Fig. 9C**). The method for determining the affinity was as follows. Thermofisher Capture Select™ Biotin anti-IgG-Fc (Hu) (diluted PBS buffer) was immobilized on neutravidin coated Bionetic label-free microarray plate at 5 ug/ml until binding reached equilibrium. Plate subsequently was washed 3X with 0.1% BSA, 0.1% Tween20, PBS dilution/wash buffer. ABX0020 (5 ug/ml in dilution/wash buffer) was captured by anti-IgG-Fc until binding reached equilibrium. Plate was subsequently washed in dilution/wash buffer 3X. V-0025 HLA-E 01:03 monomer complex (serial dilutions starting at 5 ug/ml in dilution/wash buffer) was added to wells and allowed to incubate for 20 minutes to determine the binding association and then immediately followed by dissociation (dilution/wash buffer) for approximately 25 minutes. Binding affinity calculated using Tracedrawer kinetic analysis software.

[00252] ABX0020 detection sensitivity could be observed by ELISA. In brief, V-0034 HLA-E 01:03 monomer complex (serial dilutions starting at 2 µg/ml in 0.1% BSA, 0.1% Tween20, PBS buffer) was immobilized on neutravidin coated microarray plate for one hour at RT. Plate was

subsequently washed in dilution/wash buffer 5X. Antibodies were diluted to 1 µg/ml in dilution/wash buffer and incubated for one hour at RT and subsequently washed in dilution/wash buffer 5X. Anti-mouse and anti-human HRP conjugate was diluted 1:5000 in dilution/wash buffer and incubated for 30 minutes at RT and then subsequently washed 5X in dilution/wash buffer. TMB substrate incubated for 15 minutes at 50 µL/well. 1N HCl stop solution added at 50 µL/well and plate is read at 450 nm. In **Fig. 9D**, ABX0020 and HLA-E were bound at 1 µg/mL and tested against a titration of the antigen V-0034. Similarly, in **Fig. 9E**, V-0034 was bound at 0.25 µg/mL and tested against a titration of ABX0020 and HLA-E using a similar ELISA protocol as described for **Fig. 9D**. To check stability, ABX0020 was left at 37°C for 7 to 14 days, then checked against ABX0020 stored at 4°C. ABX0020 was diluted to 1 µg/ml in mouse serum incubated at 37°C for 7 and 14 days (4°C control was prepared in serum at time of testing) and added to wells with immobilized HLA-E 01:03 monomer complexes and run in an ELISA as described above. As shown in **Fig. 9F**, binding was not altered, indicating good stability of ABX0020.

[00253] To further characterize specificity, K-562 cells transfected to express HLA-E (K562.E) were peptide-pulsed with an array of peptides, then tested for binding to HLA-E and ABX0020. As shown in **Fig. 9G**, all peptides pulsed showed loading, based on an increase in HLA-E expression compared with no peptide (unpulsed). ABX0020 showed specificity for classical HLA and the non-classical HLA signal peptide HLA-G loaded on HLA-E, with no binding to the three additional peptides tested (**Fig. 9H**). An alanine scan based on the peptide sequence for V-0025 (HLA-G signal peptide) indicated that the binding of ABX0020 to peptide/HLA-E complex is mainly dependent on the peptide at position 8 and position 9 (**Fig. 9I**). Overall, these results indicate that ABX0020 exhibits broad selectivity, to classical HLA peptide signal sequences and to non-classical HLA-G peptide signal sequence, with high affinity and stability.

Example 3. ABX0020 binds with selectivity to target positive cancer cell lines

[00254] To confirm specificity, binding of ABX0020 was tested in a variety of tumor cell lines. Since HLA-E is known to be highly expressed in normal placenta trophoblasts, the choriocarcinoma trophoblastic cell line JEG-3 was used as a positive control for binding by both HLA-E and ABX0020 (**Fig. 11A**). To confirm the restriction of ABX0020 to HLA-E/peptide complexes, binding was tested in HLA-E-deficient JEG-3 (JEG-3 Eko). As shown in **Fig. 11A**, middle panel, HLA-E and ABX0020 were unable to bind to JEG-3 Eko cells. To confirm that ABX0020 only recognizes canonical peptide/HLA-E complexes requiring TAP expression, binding

was tested in Tap-1 knock-out JEG-3 cells (JEG-3 Tap-1ko). As shown in **Fig. 11A**, lower panel, there is still some expression of HLA-E without Tap-1, however, ABX0020 exhibits no binding, indicating that it only recognizes signal peptides being processed via the conventional pathway, i.e. classical and non-classical HLA I signal peptides. Specificity was similarly shown using K-562 cells. The wild type (WT) does not express HLA-E, however, once HLA-E is knocked-in, binding is observed by both HLA-E and ABX0020 (**Fig. 11B** top and middle panels). This is because K562.E cells express cytoplasmic levels of endogenous HLA proteins, HLA-A*1101 and HLA-C*w05. Binding is further increased when the HLA-E+ K-562 cells are pulsed with the peptide V-0025 (**Fig. 11B** lower panel). Peptide loading studies were performed by pulsing K562.E cells with 2 μ M of peptide for 2 hours to overnight before usage for cell staining. These data again illustrate the specificity of ABX0020 for HLA-E+ cells.

[00255] HLA-E is known to be increased in multiple types of cancers. Therefore, a broad range of cancer cell lines were analyzed for HLA-E expression and ABX0020 binding. Since HLA-E can be upregulated when cells are stressed or stimulated, binding was observed in both unstimulated and IFN γ -stimulated cells. **Fig. 11C** illustrates cell lines that express HLA-E and bind ABX0020 without stimulation, however, stimulation often increases binding. Interestingly, these cells were all are of leukocyte origin, including THP-1 (acute myeloid leukemia), RPMI 8226 (multiple myeloma) and JY-A2 (EBV-transformed B lymphoblastoid cell). Cell lines that required stimulation for ABX0020 binding include COLO 205 (Colorectal adenocarcinoma), PANC-1 (pancreatic epithelial carcinoma), A549-D5 (lung carcinoma) and JVM-2 (EBV-transformed lymphoblast) (**Fig. 11D**). These results indicate that ABX0020 may be used to target multiple types of cancer. The K-562, THP-1, RPMI-8226, COLO205, PANC-1, JVM-2 cells were acquired from ATCC. K-562 cells expressing HLA-E (K562.E), JY-A2 and mutated JEG3 cells were acquired from (Thorald van Hall; Leiden University Medical Center). A5495-D5 were A549 cells acquired from ATCC that were altered to express HLA-E using Crisper-Cas9 technology (Applied Stem Cell, CA). In some instances, cells required stimulation overnight with IFN γ (10ng/ml) to induce HLA-E expression.

[00256] For all cell binding studies, cells were blocked with anti-human CD16 (clone KD1), anti-human CD32 (clone AT10), and anti-human CD64 (clone 10.1) (Bio-Rad) or with Human TruStain FcX (BioLegend) at room temperature for 5-10 min before surface staining with ABX0020 or hIgG1 (clone QA16A12, BioLegend) at 1 μ g/mL or with AF647-labeled ABX0020 or hIgG1, and with HLA-E in PE or PE-Cy7 (clone 3D12, BioLegend) at 4°C for 30 min in 100 μ L. Cells were

then washed with staining buffer (PBS with 2mM EDTA) followed by secondary staining cocktail including Goat-anti-human(GAH)/APC (Jackson ImmunoResearch) and zombie/aqua viability stain (BioLegend). Cells were incubated at 4°C for 30 min in 100µL. Cells were washed twice with staining buffer and fixed using fluorofix (BioLegend). Samples were acquired using an LSR II flow cytometer (BD Biosciences) or a CytoFLEX S (Beckmen Coulter). Data was prepared using Flowjo Software version 10 (BD Biosciences).

Example 4. ABX0020/21/22 improve the cytotoxicity of NK cells through blocking the HLA-E: NKG2A checkpoint pathway

[00257] The receptor, NKG2A is generally expressed on up to 60% of NK cells in peripheral blood and the frequency of NKG2A+ NK cells has been reported to be as high as 90% in the tumor microenvironment. The primary objective of these studies was to determine the ability of ABX0020 and derivatives ABX0021 and ABX0022 to inhibit the HLA-E:NKG2A axis by binding to HLA-E/signal peptide complexes expressed on tumor cells to unleash NK cell mediated killing. To test the ability of ABX0020 to block the HLA-E/NKG2A inhibitory axis, primary human NK cells were co-cultured with various tumor target cells in the presence of ABX0020. Blood from healthy volunteers was acquired from Carter BloodCare. PBMCs were isolated by density-gradient centrifugation using Ficoll-Paque PLUS (GE Healthcare) or Lymphoprep (StemCell Technologies). Natural Killer (NK) cells were purified using EasySep human NK cell enrichment kit (StemCell Technologies).

[00258] Since IgG1 can stimulate Fc receptors, ABX0020 was also tested as a-glycosylated (ABX0021) and with enhanced antibody-dependent cellular cytotoxicity (ADCC) activity (ABX0022). As shown in **Fig. 12A**, after four-hour co-culture of NK cells with IFN γ -stimulated and peptide-pulsed JY-A2 cells, ABX0020 and ABX0022 were able to significantly increase killing of JY-A2 (**Fig. 12A**) and upregulate NK CD107a expression (**Fig. 12B**). ABX0021 exhibited increased killing when tested over a longer period of time. ABX0021-mediated killing of both unstimulated (**Fig. 12C**) and IFN γ -stimulated and peptide-pulsed JY-A2 cells (**Fig. 12D**) after 24 hour co-culture. Similar results were also found when using K562.E cells (**Fig. 12E**). The performance of ABX0021 compared with ABX0020 and ABX0022 was also evident when tested in NK cells co-cultured with unstimulated RPMI 8226 cells for 24 hours (**Fig. 12F**). To show a dose-dependent effect, ABX0020 and ABX0022 were titrated from 10 µg/mL to 0.1 µg/mL in NK cells co-cultured with IFN γ -stimulated and peptide-pulsed JY-A2 cells (**Fig. 12G**). Since ABX0022 was mutated to have

enhanced ADCC effect, it exhibited a much greater killing and activation (measured by CD107a) effect than ABX0020 even at 0.1 $\mu\text{g/mL}$ (**Fig. 12H**), however both showed a significant improvement compared with targeting NKG2A on the surface of NK cells.

[00259] Finally, to test the potential synergistic effect of the ABX0020 family, ABX0020 and ABX0021 were used alone or in combination with cetuximab (anti-EGFR) in NK cells co-cultured with COLO 205 target cells. ABX0020 alone exhibited greater killing enhancement compared with ABX0021. ABX0021 was able to act in combination with cetuximab to significantly improve killing over cetuximab alone (**Fig. 12I**).

[00260] These results indicate that ABX0020 can be used to promote NK cell activation and cytotoxicity by blocking the HLA-E:NKG2A axis. Furthermore, ABX0020 and derivatives can act through additional pathways, including through ADCC activity and in combination with additional antibody therapeutics.

Example 5. ABX0020 and ABX0021 improve the target killing mediated by antigen-specific CTLs through blocking the HLA-E:NKG2A axis

[00261] Tumor infiltrating CD8+ T-cells upregulate expression of the NKG2A inhibitory receptor and T-cell suppression mediated via this pathway is reversible using antibodies to NKG2A. Furthermore, anti-tumor responses are mediated by CD8+ T-cells in mouse tumors lacking Qa-1b but not against tumor cells expressing Qa-1b. Shown herein are results that exemplify ABX0020 disrupts the HLA-E:NKG2A inhibitory pathway by binding to HLA-E/peptide complexes to unleash T cell effector functions.

[00262] To establish ABX0020 as a checkpoint blocking antibody with the ability to enhance antigen-specific T-cell responses, Flu-specific CD8+ T cells were used in co-culture assays with JY-A2 target cells to measure T-cell lytic activity. In brief, JY-A2 cells expressing PD-L1, HLA-E, and HLA-A2 were pulsed with the specific flu peptide, M1, with cytolytic activity measured in a Calcein-AM release assay. An anti-M1/flu-specific T cell line was provided by Dr. Thorbald van Hall while a second CTL line to the same M1/HLA-A2 target was purchased from Astarte Biologics (Catalog No. 1039). Prior to running the cytotoxic assays, T cells were expanded over 10 days with ImmunoCult human CD3/CD28 T cell activator in ImmunoCult-XF-T cell expansion medium supplemented with human recombinant IL-2 (10 ng/mL) and IL-15 (20 ng/mL) using standard protocol provided with ImmunoCult-XF T cell Expansion Medium (Catalog 10981, StemCell Technologies). JY-A2 cells were stimulated with IFN γ overnight and then pulsed for one hour with

the M1-flu peptide followed by staining with Calcein-AM (1.0 μ M/mL) before co-culturing with CD8+ T cells. Co-cultures were incubated with and without anti-NKG2a, ABX0021, ABX0020 or isotype control antibody. Specific lysis was calculated according to the formula [(test release - spontaneous release)/(maximum release - spontaneous release)] x 100. Spontaneous release represents Calcein-AM release from target cells in medium alone, and maximum release is the Calcein-AM release from target cells lysed in medium 2% Triton X-100, each measured in at least three replicate wells. The data shown are the frequencies of JY-A2 target cell lysis. p values are calculated by using unpaired student t-test; results are in mean $\pm$ -SD.

[00263] All statistical analysis was performed using GraphPad Prism software version 8 (GraphPad). Statistical significance was determined using Wilcoxon matched-pairs signed rank test. Significance was set at $p < 0.05$.

[00264] As shown in **Fig. 13**, CD8+ T cells in presence of isotype control (Mab Control) or without antibody (None) displayed no significant killing due to T-cell inhibition via interaction with HLA-E/signal peptide complexes. In contrast, a significant increase in target cell lysis was observed in culture wells with the addition of α NKG2A, ABX0020 or ABX0021. The cytolytic activity of two different CD8+ T cell lines (**Fig. 13**) exhibited approximately a 2-fold increase in target cell lysis in presence of α NKG2A, ABX0020 and ABX0021 compared to MabCtrl and showed approximately a 4-fold increase in target cell lysis compared to the "None" control. No difference between donors was observed for target cell lysis in the presence of ABX0020, ABX0021 (a-glycosylated) or α NKG2A.

[00265] These data demonstrate the HLA-E:NKG2A pathway inhibits T-cell cytolytic activity and that blocking this pathway using ABX0020 can reverse the suppression and unleash target (tumor) cell killing by CD8+ T-cells.

Example 6. Creating a bispecific antibody capable of both activating T-cells and blocking the HLA-E:NKG2A axis to release suppression of NK and T-cells

[00266] ABX0040 was constructed as a bispecific antibody to be able to activate CD3+ T-cells and simultaneously inhibit the HLA-E:NKG2A checkpoint pathway. ABX0040 was made as an Fab-Fc-scFv construct containing ABX0020 (Fab) coupled to a single-chain (scFv) of clone SP34 (mouse anti-human CD3e) on a non-glycosylated (N297D mutation) human IgG1 scaffold (**Fig. 14A**). A 20 amino acid linker (GKPGSGKPGSGKPGSGKPGS) was used to covalently join the ABX0020 Fab with the SP34 scFv. ABX0040 was produced in a transiently transfected CHO cell

and purified on a Protein-A affinity column. ABX0040 was run on a reducing SDS-PAGE gel and shows the expected two bands at the anticipated MW (25kD for the ABX0020 light chain and ~55kD for ABX0040 without light chain). Greater than 91% of ABX0040 migrates as a single peak on an analytical SEC-HPLC column (**Fig. 14B**).

[00267] The binding affinity of ABX0040 was determined using a label-free assay (ResoSens instrument, Resonant Sensors, Inc). Briefly, V-0025 HLA-E 01:03 monomer complex (diluted in 0.1% BSA, 0.1% Tween20, PBS buffer) was immobilized on neutravidin coated Bionetic label-free microarray plate at 5 µg/ml until binding reached equilibration. Plate was subsequently washed in dilution/wash buffer 3X. The ABX0040 (serial dilutions starting at 10 µg/ml in dilution/wash buffer) binding association was evaluated for approximately 20 minutes and immediately followed by dissociation (dilution/wash buffer) for approximately 15 minutes. Binding affinity calculated using Tracedrawer kinetic analysis software. The findings revealed a dissociation equilibrium constant of 1.57 nM (**Fig. 15**).

[00268] *Binding properties of ABX0040:* ABX0040 binding to target tumor cells was first confirmed. As shown in **Fig. 16**, ABX0040 binds to wild type (WT) JEG3 cells similarly to the parent clone (ABX0023). This binding is HLA-E restricted, as HLA-E knock-out JEG3 cells do not exhibit binding to ABX0040 (**Fig. 16A-Fig. 16B**). This was confirmed using THP-1 cells stimulated overnight with IFN γ to upregulate HLA-E expression (**Fig. 17**). Binding to T cells in peripheral blood mononuclear cells (PBMCs) was used to confirm the anti-CD3 arm (**Fig. 18A-Fig. 18E**). JEG3, THP-1, K-562, and RPMI 8226 cell lines were acquired from ATCC. K-562 cells expressing HLA-E and HLA-E knock-out JEG3 cells were acquired from (Dr. Thorbald van Hall, Leiden University Medical Center, Netherlands). Cells were cultured per the supplier's recommendation. For cell binding, cells were blocked with anti-human CD16 (clone KD1), anti-human CD32 (clone AT10), and anti-human CD64 (clone 10.1) (Bio-Rad) or with Human TruStain FcX (BioLegend) at room temperature for 5-10 min before surface staining with unlabeled antibody at 1µg/mL or with AF647-labeled antibody, and with HLA-E/PE-Cy7 (clone 3D12, BioLegend) at 4°C for 30 min in 50-100µL. Cells were then washed with staining buffer (PBS with 2mM EDTA) followed by secondary staining cocktail including Goat-anti-human or Goat-anti-mouse/AF647 (if using unlabeled antibody, Jackson ImmunoResearch) and zombie/aqua viability stain (BioLegend). Cells were incubated at 4°C for 30 min in 50µL. Cells were washed twice with staining buffer and fixed using fluoroxif (BioLegend). Samples were acquired using a CytoFLEX S (Beckmen Coulter). Data was prepared using FlowJo Software version 10 (BD Biosciences).

[00269] *ABX0040 enhances target-specific cytotoxicity of primary CTLs:* To assess the activity of ABX0040, primary human CTLs were co-cultured with either parent K562 (HLA-E negative) or K562.E (HLA-E positive) and tested with a titration of ABX0040. As shown in **Fig. 19A**, ABX0040 induced dose-dependent cytotoxicity in a target-specific manner; HLA-E negative cells (K562 parent) were not affected. ABX0040 also induced expression of CD107a (24 hrs) (**Fig. 19B**) and IFN γ (48 hrs) (**Fig. 19C**) in CD8+ T cells cultured with target-positive tumor cells.

[00270] These results were confirmed using THP-1 cells (binding data shown in **Fig. 17**). After 48 hr co-culture, ABX040 induced cytotoxicity in a dose-dependent manner (**Fig. 20A**). ABX0040 was also able to induce CD8+ T cell activation, as shown by the dose-dependent induction of CD25, CD107a, perforin and IFN γ (**Fig. 20B-Fig. 20E**). These results indicate that ABX0040 can enhance lysis of tumor cells by CD8+ T cells in a target-specific manner.

[00271] To perform in vitro T-cell activation assays, blood from healthy volunteers was acquired from Carter BloodCare (Arlington, TX). PBMCs were isolated by density-gradient centrifugation using Ficoll-Paque PLUS (GE Healthcare) or Lymphoprep (StemCell Technologies). CD8+ T cells were purified using EasySep human CD8+ T cell enrichment kit (StemCell Technologies). The enriched human CD8+ T cells (CTLs) were rested overnight at 1×10^6 /mL. Target cells were labeled with CFSE (ThermoFisher) and added to the rested CTLs at a ratio of 10:1 (E:T). CD3/CD28 stimulation (ImmunoCult human CD3/CD28 T cell activator, StemCell Technologies) was used as a positive control. In the last 4 hr of culture, monensin and anti-human CD107a/BV421 (BioLegend) was added to all wells. Cells were harvested after 24 to 48 hrs. Cells were stained with anti-human CD8/APC (BioLegend), anti-human CD25/PE-Cy7 (Tonbo) and Zombie/Aqua viability marker (BioLegend). For intracellular staining, cells were fixed and permeabilized using BD cytofix/cytoperm solution (BD) and were stained with anti-human Perforin/PerCP-Cy5.5 (BioLegend) and anti-human IFN γ /PE-Dazzle 594 (BioLegend). Samples were acquired using a CytoFLEX S (Beckmen Coulter). Data was prepared using FlowJo Software version 10 (BD Biosciences).

[00272] As the parent antibody (ABX0021) has been shown to act as a checkpoint blocker in the HLA-E/NKG2A axis, the checkpoint blocking activity of ABX0040 was assessed. As shown in **Fig. 21A-Fig. 21B**, both ABX0040 and ABX0021 enhanced the cytotoxicity of NK cell co-cultured with K562.E and RPMI 8226 cells. NK cells used for these assays were purified using EasySep human NK cell enrichment kit (StemCell Technologies). The assays were performed using human NK cells incubated at 1×10^6 /mL with IL-2 (R&D systems). After overnight stimulation, CFSE

(Thermo Fisher)-labeled target cells were added at a ratio of 3:1 (E:T). Antibodies were used at 10 µg/mL. Supernatant was tested for lactate dehydrogenase (LDH, Roche). The plate was read at 450 nM using a BioTek Synergy 2 plate reader (Agilent). These results indicate that ABX0040 can act as a checkpoint blocker on NK cells in addition to enhancing cytotoxicity in CD8+ T cells.

Table 4. List of peptide/HLA complexes

Peptide family	Peptide ID	Sequence	HLA complex	Gene Origin
Classical HLA	V-0021	VMAPRTLIL	HLA-E	HLA-C HLA-Cw*01, -Cw*03, -Cw*04, -Cw*05, -Cw*06, -Cw*08, -Cw*12, -Cw*14, -Cw*16 and -Cw*17:02
	V-0034	VMAPRTLVL	HLA-E	HLA-A*02, -A*23, -A*24, -A*25, -A*26, -A*34:02, -A*34:06, -A*43, -A*66 and -A*69
	V-0035	VTAPRTLLL	HLA-E	HLA-B*13, -B*18, -B*27, -B*37, -B*40, -B*44, -B*47, -B*54, B*55, -B*56, -B*59, -B*82 and B*83
	V-0037	IMAPRTLVL	HLA-E	HLA-A*34:01
	V-0040	VMAPQALLL	HLA-E	HLA-Cw*17:01, Cw*17:03 and -Cw*17:05
	V-0041	VMAPRALLL	HLA-E	HLA-Cw*06:17, -Cw*07 and -Cw*18
	V-0042	VMAPRTLIL	HLA-E	HLA-A*01, -A*03, -A*11, -A*29, -A*30, A*31, -A*32, -A*33, -A*36, and A*74, HLA-Cw02 and Cw*15
	V-0043	VMAPRTLTL	HLA-E	HLA-Cw*08:09
	V-0044	VMAPRTVLL	HLA-E	HLA-B*07, -B*08, -B*14, -B*38, -B*39, -B*42, -B*48, -B*67, -B*73 and -B*81
	V-0045	VMPPRTLLL	HLA-E	HLA-A*80
	V-0046	VTAPRTVLL	HLA-E	HLA-B*15, -B35, -B*40, -B*41, -B*44:18, -B*45, -B*46 -B*49, -B*50, -B*51, -B*52, -B*53, -B*57, -B*58 and -B*78
Non-classical HLA	V-0025	VMAPRTLFL	HLA-A2*02:01 And HLA-E	HLA-G, HLA-G*01
Additional	LL-001	VTVPPGPSL	HLA-E	PIP5K1A and PSMD4 like (pseudogene)
	LL-002	SLLEKSLGL	HLA-E	Chain B, Eukaryotic Translation Elongation Factor 1 Epsilon-1
	V-0013	ILSPTVVS	HLA-E	KIF11
	V-0038	QMRPVSRVL	HLA-E	Hsp60
	P-0550	RAARLPPLL	HLA-E	PODXL2
	0002-A2	SLIQHLIGL	HLA-A2*02:01	PRAME
	0003-A2	KLQCVDLHV	HLA-A2*02:01	KLK3
	V-0018	YLLPAIVHI	HLA-A2*02:01	DDX17
Mouse analog	Qdm-Qa1b	AMAPRTLLL	Qa-1(b)	Qdm

Example 7 ABX0023 does not bind to immune cells in the periphery

[00273] In order to test binding of ABX0023 to immune cells, immune cells were purified, cultured, stained, and assessed by Flow Cytometry as described below.

Human primary cells

[00274] Blood from healthy volunteers was acquired from Carter BloodCare. PBMCs were isolated by density-gradient centrifugation using Ficoll-Paque PLUS (GE Healthcare) or

Lymphoprep (StemCell Technologies). Total T cells were purified using EasySep human T cell isolation kit (StemCell Technologies). Natural Killer (NK) cells were purified using EasySep human NK cell enrichment kit (StemCell Technologies). Neutrophils were purified using EasySep direct human neutrophil isolation kit (StemCell Technologies). Eosinophils were purified using EasySep direct human eosinophil isolation kit (StemCell Technologies). Dendritic cells (DCs) were purified using EasySep human pan-DC pre-enrichment kit (StemCell Technologies). Monocytes (MO) were purified using either EasySep human monocyte isolation kit or EasySep human monocyte enrichment kit without CD16 depletion (both from StemCell Technologies). Platelets were enriched during PBMC processing by collecting supernatant after washing PBMCs after density-gradient separation.

[00275] When stimulating overnight with IFN γ , PBMCs were cultured at 1×10^6 cell/mL in RPMI-640 medium (ATCC) supplemented with 1% penicillin-streptomycin, HEPES buffer, 2 mM L-glutamine, 1% nonessential amino acids, sodium pyruvate and 10% fetal bovine serum (Millipore Sigma). IFN γ was given at 10 μ g/mL and compared against PBMCs without IFN γ .

Cell Lines

[00276] HT-1376, SKBR3, SU.86.86, RPMI-8226, THP-1, OVCAR3, LNCaP, NCI-H1355, COLO205, PANC-1, HCT-116, A549, and JEG-3 cells were acquired from ATCC. NCC-STC-K140 and RCC-10RGB cells were acquired from Sekisui XenoTech. SNU-899 cells were acquired from the Korean cell line bank. OCI-AML3 cells were acquired from DSMZ. JEG-3 HLA-E^{KO} and Tap1^{KO} cells and OCI-AML3 HLA-E^{KO} were acquired from Professor Throbald van Hall. Some cells were stimulated for 24 hours with IFN γ (10 μ g/mL).

Macrophage Differentiation

[00277] Macrophages were generated by culturing monocytes in Immunocult-SF macrophage medium supplemented with 5 μ g/mL M-CSF (StemCell Technologies). Additional medium was added on day 4. M0 macrophages were activated on day 6 using LPS (10 ng/mL) and IFN γ (50 ng/mL) for M1 activation or IL-4 (10 ng/mL) for M2a activation. M1 and M2a macrophages were harvested after 2 days of activation. For dissociation, accutase was used for M1 macrophages and 2.5 mM EDTA was used for M2a macrophages.

Flow Cytometry

[00278] ABX0023, mIgG1 and MEM-E/02 were labeled with AlexaFluor 647 (AF647) using SiteClick Antibody Azido Modification kit and Click-iT AF647 sDIBO alkyne antibody labeling kit (Thermo Fisher Scientific).

[00279] For cell binding using unlabeled antibodies, cells were stained with ABX0023, ABX0020, mouse isotype IgG1 (MOPC-21, BioLegend), human isotype IgG1 (QA16A12, BioLegend), 3D12 (BioLegend), or MEM-E/02 (BioRad) at 1 to 5µg/mL at 4°C for 30 min in 100µL. Cells were then washed with staining buffer (PBS with 2mM EDTA) followed by secondary staining cocktail including Goat-anti-human/AF647 (Jackson ImmunoResearch) or goat-anti-mouse/AF647 (Thermo Fisher Scientific) and zombie/aqua viability stain (BioLegend). Cells were incubated at 4°C for 30 min in 100µL. Cells were washed twice with staining buffer and acquired in 100µL of staining buffer. For cell binding using labeled antibodies, cells were incubated with antibody staining cocktail at 4°C for 30 min in 100µL, followed by washing twice with staining buffer and acquisition in 100µL of staining buffer. Some cells required Fc receptor blocking prior to staining by incubating for 5-10 min at room temperature with human TruStain FcX Fc receptor blocking solution (BioLegend). If cells were unable to be acquired on the same day as staining, they were fixed using 100µL of FluoroFix buffer (BioLegend). Samples were acquired using a CytoFLEX S (Beckmen Coulter). Data was prepared using Flowjo Software version 10 (BD Biosciences).

[00280] Anti-HLA-E(3D12)/PE-Cy7, anti-CD3(HIT3a)/APC-Cy7, anti-CD4(RPA-T4)/PerCP-Cy5.5, anti-CD8(RPT-T8)/BV605, anti-CD14(M5E2)/FITC, anti-CD16(3G8)/PacificBlue, anti-CD19(HIB19)/FITC, anti-CD20(2H7)/BV421 anti-CD56 (5.1H11)/AF700, anti-Siglec-8(7C9)/PE and anti-HLA-A,B,C (W6/32)/AF488 were purchased from BioLegend. Anti-CD56(B159)/PE-CF594 was purchased from BD BioScience. Anti-CD3(HIT3a)/FITC and anti-CD4(OKT4)/PE were purchased from Tonbo Biosciences.

[00281] Since immune cells are known to express HLA-E and classical HLA type I, they were tested for binding to ABX0023. While all immune cell subsets aside from platelets and DCs express HLA-E, only NK cells, monocytes (MO) and MO-derived macrophages exhibited binding by ABX0023 (**Fig. 22**), however this may be donor dependent. Since HLA-E can be upregulated when cells are stressed or stimulated^{9, 10}, ABX0023 binding in PBMCs was tested with and without IFN γ stimulation. While HLA-E clone 3D12 did exhibit a slight increase in binding with stimulation, only HLA-E clone MEM-E/02, which recognizes HLA-E without peptide or B2M (heavy chain specific), was upregulated; there was no change in ABX0023 binding (**Fig. 23**). This data indicates that ABX0023 should have little if any off-target activity on immune cells in the periphery.

Example 8 ABX0023 binding requires HLA-E and classical HLA type I expression

[00282] To identify tumor cell lines that bind to ABX0023, various cell lines were analyzed for their expression of HLA-E and HLA-A,B,C (classical HLA type I). Two types of cell lines were observed: cell lines that bind ABX0023 without stimulation (**Fig. 24 and 25**) and cell lines that require IFN γ -stimulation for ABX0023 binding (**Fig. 26**). Cell lines that bind to ABX0023 without stimulation (**Fig. 24**) show an increase in ABX0023 binding with IFN γ -stimulation (**Fig. 25**). Interestingly, some cell lines express high levels of both HLA-E and HLA-A,B,C, but do not exhibit any ABX0023 binding without stimulation (**Fig. 26**).

[00283] HLA-E selectivity was confirmed by testing tumor cell lines that express classical HLA type I but not HLA-E (**Fig. 27**). Additional selectivity of ABX0020/23 to HLA-E complexes was confirmed by testing isogenic cell lines. As shown in **Fig. 28A**, middle panel, HLA-E and ABX0020/23 were unable to bind to JEG-3 E^{ko} cells. To confirm that ABX0020/23 only recognizes canonical peptide/HLA-E complexes requiring TAP expression, binding was tested in Tap-1 knock-out JEG-3 cells (JEG-3 Tap-1^{ko}). As shown in **Fig. 28A**, right panel, there is still some expression of HLA-E without Tap-1, however, ABX0020/23 exhibits no binding, indicating that it only recognizes peptides being processed via the classical pathway, i.e. classical and non-classical HLA peptides. Similar results were observed using HLA-E-deficient OCI-AML3 (**Fig. 28B**).

Example 9 Validation of staining protocol using frozen cell blocks

[00284] In order to analyze immunohistochemistry (IHC) staining of tissue samples, IHC staining was tested on frozen cell blocks. Blocks of human frozen tissue (tumor and normal adjacent tissue (NAT)) were purchased from ProteoGenex (Inglewood, CA) and embedded in OCT compound. Samples were sectioned using a microtome-cryostat and mounted on slides. Immunohistochemistry (IHC) staining was performed by NovoVita Histopath Laboratory, LLC. (Cambridge, MA). Briefly, frozen tissue slides were air dried for 20 minutes before being wet loaded onto the Ventana XT discovery ultra-instrument (Ventana Medical Systems, Tucson, AZ). Slides were then rinsed with 1x Ventana Reaction buffer (Cat.#950-300) before treating with peroxidase inhibitor CM (Ventana) for 12 min to block endogenous peroxidase. After rinsing with 1x Ventana Reaction buffer, slides were warmed to 37°C and incubated with 2.25 μ g/ml of primary antibody (anti-HLA-E (MEM-E/02, AbCam), mouse IgG1 isotype control, or ABX-0023) for 60 min. Slides were rinsed 3x with Ventana Reaction buffer and incubated with FineFix working solution (Milestone, Kalamazoo, MI, Cat. #70147WG) for 4 min (post-fixation step) and rinsed 3x. Discovery anti-mouse HQ (Ventana, Cat. #760-4814) was applied to slides for 24 min, rinsed 3x

using Ventana Reaction buffer. One drop of DISC anti-HQ HRP (Ventana, Cat.#760-4820) was applied to slides, incubated for 24 min and rinsed 3x with Ventana Reaction buffer. Next, one drop of Discovery ChromoMap DAB kit (Ventana, Cat.#760-159) and one drop of CM H₂O₂ (Ventana) was applied to slides, incubated for 8 min followed by rinsing 3x with Ventana Reaction buffer. Then one drop of copper CM (Ventana) was applied to slides, incubated for 4 min followed by rinsing 3x with Ventana Reaction buffer before applying one drop of Hematoxylin (counterstain) to slide for 12 min. Following rinsing (2x) with Ventana Reaction buffer one drop of Bluing Reagent (post counterstain) was applied and after 8 min slides were rinsed 2x with Ventana Reaction buffer. Slides were then removed from Ventana XT, washed with dishwash detergent and treated with alcohol and xylene for dehydration. A coverslip was added to slides and slides were read on Discovery Ultra instrument.

[00285] ABX0023 (ABX0020 substituted with mouse IgG1), anti-HLA-E (MEM-E/02) antibody and mouse IgG1 isotype control antibody were used at 2.25 ug/ml to stain cell blocks of K562 cells or K562 cells transfected with HLA-E (K562.E) pulsed for 2 hr with 20ug/ml of V-0025 (VMPRTLFL) peptide (**Fig. 29**). Images show that ABX-0023 stains strong (3+++ out of 3) to K562.E + V-0025 peptide pulsed cells and not to K562 cells (-). These data show that ABX-0023 is binding selectively to cells presenting HLA-E/V-0025 and validates the immunohistochemistry (IHC) staining protocol.

Example 10 Staining positive control tissue

[00286] Fresh frozen human placenta tissue was used as a positive control for ABX-0023. It is well known that trophoblast cells express both HLA-E, and some classical HLA I such as HLA-C and HLA-G. Therefore, staining with ABX-0023 was anticipated in placental tissue. In **Fig. 30**, ABX-0023 shows strong (2++ to 3+++) staining of trophoblast cells in placenta tissue and demonstrates that the HLA-E + canonical leader sequence peptides are present on the surface of trophoblastic cells.

Example 11 ABX-0023 stains head and neck tumor tissue

[00287] To assess ABX-0023 target binding selectivity in head and neck tumor tissues, tissue was stained and analyzed as described below. **Fig. 31** is a representative image of ABX-0023 staining frozen tumor tissue collected from a head and neck patient. **Fig. 31A** left panel shows strong tumor cell staining with anti-HLA-E antibody (clone MEM-E/02). The same panel shows

staining of stroma area with MEM-E/02 antibody. Right panel shows ABX-0023 antibody staining of tumor tissue. Tumor stroma shows strong staining (3+++) while tumor cells show weak to moderate staining. Images indicate that the target, HLA-E + leader sequence from classical HLA Class I or non-classical HLA-G is present in tumor tissue of head and neck cancer patients. **Fig. 31B** shows an image of normal adjacent tissue (NAT) stained with MEM-E/02 (left) and ABX0023 (right). Note that NAT epithelium is positive for HLA-E expression (left), however absence of ABX-0023 staining indicates lack of HLA-E/peptide complex in NAT epithelium (right).

Example 12 ABX-0023 stains colon adenocarcinoma tumor tissue

[00288] To assess ABX-0023 target binding selectivity in colon adenocarcinoma tumor tissues, tissue was stained and analyzed as described below. A representative image showing fresh frozen human colon adenocarcinoma tissue stained with anti-HLA-E (left; 10x magnification) or ABX-0023 (right; 10x magnification). **Fig. 32A** shows HLA-E expression in both tumor and stroma areas (left) and HLA-E/leader sequence complexes detectable in both tumor (2++) and stroma (3+++) areas. **Fig. 32B** shows ABX-0023 does not stain normal colon tissue and weakly stains (1+) mucosa tissue.

Example 13 ABX-0023 stains lung squamous carcinoma tissue

[00289] To assess ABX-0023 target binding selectivity in lung squamous carcinoma tissue, tissue was stained and analyzed as described below. A representative image shows fresh frozen lung squamous carcinoma tissue stained with anti-HLA-E (left, top 10x magnification) or ABX-0023 (right; 10x magnification). **Fig. 33A** shows tumor and stroma staining with either anti-HLA-E antibody (2++) or ABX-0023 (1+ to 2++) indicating HLA-E and HLA-E/leader sequence peptide complex in lung cancer. **Fig. 33B** shows that ABX-0023 does not stain normal adjacent lung tissue indicating the HLA-E loaded with leader sequence peptides from classical HLA I or non-classical HLA is not present in normal lung tissue.

Example 14 Competition assay demonstrates ABX-0023 binding is specific to HLA-E loaded with leader sequence peptides

[00290] To assess ABX-0023 target binding selectivity in tumor tissue, fresh frozen sections from colon cancer tissue were stained with ABX-0023. The top panel in **Fig. 34**, shows ABX-0023 staining both tumor and stroma in colon adenocarcinoma tissue. In the bottom left panel of **Fig. 34**,

ABX-0023 is blocked from staining tumor tissue after mixture with 20ug/ml of HLA-E/V-0025 (VMAPRTLFL) peptide complex. In contrast, **Fig. 34** bottom right panel, shows ABX-0023 retains staining of tumor tissue in the presence of HLA-E/P-0550 control peptide complex.\

Example 15– Determining NK survival and function in human IL-15 transgenic NOG mice

[00291] The CD94/NK group 2 member A (NKG2A) heterodimeric receptor is one of the most prominent Natural Killer (NK) cell inhibitory receptors. Binding of ligand, HLA-E containing leader sequence peptides from classical HLA class I or HLA-G to NKG2A transduces inhibitory signaling through 2 inhibitory immune-receptor tyrosine-based inhibition motifs, suppressing NK and CD8+ T-cell cytokine secretion and cytotoxicity. To assess the therapeutic benefit of ABX0020/21/22 in vivo, human NK cells were isolated from buffy coats or from leukopaks using EasySep™ human NK cell enrichment kit (Stemcell selection protocol). Donor NK cells were stained for NKG2A receptor expression using mouse anti-human NKG2A antibody (clone Z199, Beckman Coulter), and NKG2A receptor expression ranged from 20% to 60% on average. Since human NK cells do not survive long-term in mice without addition of IL-2 or IL-15 cytokines, the human IL-15 expressing transgenic NOG mouse (Taconic) was selected and 1×10^6 freshly isolated human NK cells were injected via the tail vein. Mice were bled 2-weeks post injection and cells were stained and with a panel of antibodies that included anti-NKG2A antibody and analyzed. 79.4% of NK cells from donor 1 were NKG2A+ CD56+ CD16+ and NK cells recovered from mice 2-weeks post injection with the frequency of NKG2A+ NK cells having increased to 92.3%. NK cells from a donor 2 were 73.7% NKG2A+ before injection into mice and increased to 88.7% NKG2A+ NK cells at 2-weeks post injection. Mice were followed for 8 weeks post-injection and NKG2A+ NK cells were found to maintain levels of NKG2A+ frequency at ~90%. Liver and spleen also showed significant presence of NKG2A+ NK cells.

Example 16– In vivo validation of ABX0020/21/22 using human IL-15 transgenic NOG mice and human tumor cell lines

[00292] As shown in **Fig. 24**, many tumor cell lines constitutively express HLA-E loaded with leader sequence peptides as demonstrated by staining with ABX0023. To evaluate the blocking activity of ABX0020/21/22, human IL-15 transgenic NOG mice can be injected with one million freshly isolated human NK cells via tail vein injection. At two weeks post-injection, 1×10^6 tumor cells (i.e. NCC-STC-K140, SKBR3, SU86.86) can be injected subcutaneously into the flank of mice.

Treatment can be given intraperitoneally (ip) with ABX0020/21/22 (10mg/kg) and can commence when tumors reach a mean volume of 100mm³ (Day 0). An additional 5 doses of antibody therapy can be given via ip every third day until day 15. Mice can be weighed, and tumors measured 2x/week using digital calipers. Readout can be tumor growth inhibition.

In another example, the acute myelogenous cell line, OCI-AML3-luciferase can be injected via tail vein in human IL-15 transgenic NOG mice 2-weeks after receiving one million human NK cells. Treatment with ABX0020/21/22 (10mg/kg) can be given intraperitoneally (ip) and commence when tumors reach a mean volume of 100mm³ (Day 0). An additional 5 doses of antibody therapy can be given via ip every third day until day 15. Weekly bioluminescence readouts can be performed using an IVIS optical imaging system (Perkin Elmer). Images can be captured, and data plotted as photons/seconds and analyzed. Additionally, mice can be weighed 2x/week.

[00293] While preferred embodiments of the present invention have been shown and described herein, it will be obvious to those skilled in the art that such embodiments are provided by way of example only. Numerous variations, changes, and substitutions will now occur to those skilled in the art without departing from the invention. It should be understood that various alternatives to the embodiments described herein may be employed. It is intended that the following claims define the scope of the invention and that methods and structures within the scope of these claims and their equivalents be covered thereby.

CLAIMS

WHAT IS CLAIMED IS:

1. A monoclonal antibody or an antigen-binding fragment thereof, comprising a light chain variable domain (VL) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 7.
2. A monoclonal antibody or an antigen-binding fragment thereof, comprising a light chain variable domain (VL) comprising an amino acid sequence at least 90% identical to an amino acid sequence set forth as SEQ ID NO: 7.
3. A monoclonal antibody or an antigen-binding fragment thereof, comprising a light chain variable domain (VL) comprising an amino acid sequence at least 95% identical to an amino acid sequence set forth as SEQ ID NO: 7.
4. A monoclonal antibody or an antigen-binding fragment thereof, comprising a light chain variable domain (VL) comprising an amino acid sequence at least 99% identical to an amino acid sequence set forth as SEQ ID NO: 7.
5. A monoclonal antibody or an antigen-binding fragment thereof, comprising a light chain variable domain (VL) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 7.
6. The monoclonal antibody of any one of claims 1-5, wherein the monoclonal antibody or antigen-binding fragment thereof comprises a heavy chain variable domain (VH) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 8.
7. The monoclonal antibody of any one of claims 1-5, wherein the monoclonal antibody or antigen-binding fragment thereof comprises a heavy chain variable domain (VH) comprising an amino acid sequence at least 90% identical to an amino acid sequence set forth as SEQ ID NO: 8.
8. The monoclonal antibody of any one of claims 1-5, wherein the monoclonal antibody or antigen-binding fragment thereof comprises a heavy chain variable domain (VH) comprising an amino acid sequence at least 95% identical to an amino acid sequence set forth as SEQ ID NO: 8.
9. The monoclonal antibody of any one of claims 1-5, wherein the monoclonal antibody or antigen-binding fragment thereof comprises a heavy chain variable domain (VH) comprising an amino acid sequence at least 99% identical to an amino acid sequence set forth as SEQ ID NO: 8.

10. The monoclonal antibody of any one of claims 1-5, wherein the monoclonal antibody or antigen-binding fragment thereof comprises a heavy chain variable domain (VH) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 8.

11. The monoclonal antibody of any one of claims 1-10, wherein the monoclonal antibody or antigen-binding fragment thereof selectively binds to a complex comprising an HLA-E and a neoantigen.

12. The monoclonal antibody of any one of claims 1-11, wherein the monoclonal antibody or antigen-binding fragment thereof does not have a binding affinity to (i) the HLA-E alone; or (ii) the neoantigen alone.

13. The monoclonal antibody of any one of claims 1-12, wherein the neoantigen is expressed by an antigen processing machinery (APM)-proficient cell.

14. The monoclonal antibody of claim 13, wherein the neoantigen is expressed by a TAP1/2-proficient cell.

15. The monoclonal antibody of any one of claims 1-14, wherein the neoantigen comprises, consists essentially of, or consists of a sequence according to SEQ ID NO: 17 (VMAPRTLIL), SEQ ID NO: 18 (VMAPRTLFL), SEQ ID NO: 19 (VMAPRTLVL), SEQ ID NO: 20 (VTAPRTLILL), SEQ ID NO: 21 (IMAPRTLVL), SEQ ID NO: 23 (VMAPQALLL), SEQ ID NO: 24 (VMAPRALLL), SEQ ID NO: 25 (VMAPRTLILL), SEQ ID NO: 26 (VMAPRTLTL), SEQ ID NO: 27 (VMAPRTVLL), SEQ ID NO: 28 (VMPPTLILL), or SEQ ID NO: 29 (VTAPRTVLL).

16. The monoclonal antibody of any one of claims 1-15, wherein the neoantigen comprises, consists essentially of, or consists of a sequence according to SEQ ID NO: 17 (VMAPRTLIL), SEQ ID NO: 18 (VMAPRTLFL), SEQ ID NO: 19 (VMAPRTLVL), SEQ ID NO: 26 (VMAPRTLTL), or SEQ ID NO: 27 (VMAPRTVLL).

17. The monoclonal antibody of any one of claims 1-16, wherein the HLA-E is HLA-E*0101 or HLA-E*0103.

18. The monoclonal antibody of claim 17, wherein the antibody selectively binds to the complex comprising:

- (a) the HLA-E*0101 and the neoantigen;
- (b) the HLA-E*0103 and the neoantigen; or

(c) the HLA-E*0101 and the neoantigen, and the HLA-E*0103 and the neoantigen.

19. The monoclonal antibody of any one of claims 1-18, wherein the monoclonal antibody or antigen-binding fragment thereof is a murine antibody, a chimeric antibody, a camelid antibody, a humanized antibody, or a human antibody.

20. The monoclonal antibody of any one of claims 1-19, wherein the monoclonal antibody or antigen-binding fragment thereof is a TCR-like antibody.

21. The monoclonal antibody of any one of claims 1-20, wherein the monoclonal antibody or antigen-binding fragment thereof is a multispecific antibody.

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

23. The monoclonal antibody of any one of claims 1-22, wherein the monoclonal antibody or antigen-binding fragment thereof is a bispecific T cell engager (BiTE).

24. The monoclonal antibody of claim 23, wherein the BiTE binds to a CD3 protein associated with a T cell receptor (TCR).

25. The monoclonal antibody of any one of claims 23-24, wherein the BiTE further comprises a light chain variable domain (VL) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 15.

26. The monoclonal antibody of any one of claims 23-25, wherein the BiTE further comprises a heavy chain variable domain (VH) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 16.

27. The monoclonal antibody of any one of claims 1-26, wherein the monoclonal antibody or antigen-binding fragment thereof is a multifunctional antibody.

28. The monoclonal antibody of any one of claims 1-27, wherein the monoclonal antibody or antigen-binding fragment thereof antibody further comprises a conjugated therapeutic moiety.

29. The monoclonal antibody of any one of claims 1-28, wherein the selective binding of the antibody to the complex comprising the HLA-E and the neoantigen induces an immune response in a cell.

30. The monoclonal antibody of claim 29, wherein the immune response comprises activation of T cells.

31. The monoclonal antibody of claim 30, wherein the T cell is a CD8+ T cell.

32. The monoclonal antibody of claim 30, wherein the immune response comprises activation of cytotoxic T cells (CTLs).

33. The monoclonal antibody of claim 29, wherein the cell is a cancer cell.

34. A monoclonal antibody or an antigen-binding fragment thereof, comprising a heavy chain variable domain (VH) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 8.

35. A monoclonal antibody or an antigen-binding fragment thereof, comprising a heavy chain variable domain (VH) comprising an amino acid sequence at least 90% identical to an amino acid sequence set forth as SEQ ID NO: 8.

36. A monoclonal antibody or an antigen-binding fragment thereof, comprising a heavy chain variable domain (VH) comprising an amino acid sequence at least 95% identical to an amino acid sequence set forth as SEQ ID NO: 8.

37. A monoclonal antibody or an antigen-binding fragment thereof, comprising a heavy chain variable domain (VH) comprising an amino acid sequence at least 99% identical to an amino acid sequence set forth as SEQ ID NO: 8.

38. A monoclonal antibody or an antigen-binding fragment thereof, comprising a heavy chain variable domain (VH) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 8.

39. The monoclonal antibody of any one of claims 34-38, wherein the monoclonal antibody or antigen-binding fragment thereof comprises a light chain variable domain (VL) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 7.

40. The monoclonal antibody of any one of claims 34-38, wherein the monoclonal antibody or antigen-binding fragment thereof comprises a light chain variable domain (VL) comprising an amino acid sequence at least 90% identical to an amino acid sequence set forth as SEQ ID NO: 7.

41. The monoclonal antibody of any one of claims 34-38, wherein the monoclonal antibody or antigen-binding fragment thereof comprises a light chain variable domain (VL) comprising an amino acid sequence at least 95% identical to an amino acid sequence set forth as SEQ ID NO: 7.

42. The monoclonal antibody of any one of claims 34-38, wherein the monoclonal antibody or antigen-binding fragment thereof comprises a light chain variable domain (VL) comprising an amino acid sequence at least 99% identical to an amino acid sequence set forth as SEQ ID NO: 7.

43. The monoclonal antibody of any one of claims 34-38, wherein the monoclonal antibody or antigen-binding fragment thereof comprises a light chain variable domain (VL) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 7.

44. The monoclonal antibody of any one of claims 34-43, wherein the monoclonal antibody or antigen-binding fragment thereof selectively binds to a complex comprising an HLA-E and a neoantigen.

45. The monoclonal antibody of any one of claims 34-44, wherein the monoclonal antibody or antigen-binding fragment thereof does not have a binding affinity to (i) the HLA-E alone; or (ii) the neoantigen alone.

46. The monoclonal antibody of any one of claims 34-45, wherein the neoantigen is expressed by an antigen processing machinery (APM)-proficient cell.

47. The monoclonal antibody of claim 46, wherein the neoantigen is expressed by a TAP1/2-proficient cell.

48. The monoclonal antibody of any one of claims 34-47, wherein the neoantigen comprises, consists essentially of, or consists of a sequence according to SEQ ID NO: 17 (VMAPRTLIL), SEQ ID NO: 18 (VMAPRTLFL), SEQ ID NO: 19 (VMAPRTLVL), SEQ ID NO: 20 (VTAPRTLLL), SEQ ID NO: 21 (IMAPRTLVL), SEQ ID NO: 23 (VMAPQALLL), SEQ ID NO: 24 (VMAPRALLL), SEQ ID NO: 25 (VMAPRTLLL), SEQ ID NO: 26 (VMAPRTLTL), SEQ ID NO: 27 (VMAPRTVLL), SEQ ID NO: 28 (VMPPTLLL), or SEQ ID NO: 29 (VTAPRTVLL).

49. The monoclonal antibody of any one of claims 34-48, wherein the neoantigen comprises, consists essentially of, or consists of a sequence according to SEQ ID NO: 17 (VMAPRTLIL), SEQ ID NO: 18 (VMAPRTLFL), SEQ ID NO: 19 (VMAPRTLVL), SEQ ID NO: 26 (VMAPRTLTL), or SEQ ID NO: 27 (VMAPRTVLL).

50. The monoclonal antibody of any one of claims 34-49, wherein the HLA-E is HLA-E*0101 or HLA-E*0103.

51. The monoclonal antibody of claim 50, wherein the antibody selectively binds to the complex comprising:

- (a) the HLA-E*0101 and the neoantigen;
- (b) the HLA-E*0103 and the neoantigen; or
- (c) the HLA-E*0101 and the neoantigen, and the HLA-E*0103 and the neoantigen.

52. The monoclonal antibody of any one of claims 34-51, wherein the monoclonal antibody or antigen-binding fragment thereof is a murine antibody, a chimeric antibody, a camelid antibody, a humanized antibody, or a human antibody.

53. The monoclonal antibody of any one of claims 34-52, wherein the monoclonal antibody or antigen-binding fragment thereof is a TCR-like antibody.

54. The monoclonal antibody of any one of claims 34-53, wherein the monoclonal antibody or antigen-binding fragment thereof is a multispecific antibody.

55. The monoclonal antibody of any one of claims 34-54, wherein the monoclonal antibody or antigen-binding fragment thereof is a bispecific antibody.

56. The monoclonal antibody of any one of claims 34-55, wherein the monoclonal antibody or antigen-binding fragment thereof is a bispecific T cell engager (BiTE).

57. The monoclonal antibody of claim 56, wherein the BiTE binds to a CD3 protein associated with a T cell receptor (TCR).

58. The monoclonal antibody of any one of claims 56-57, wherein the BiTE further comprises a light chain variable domain (VL) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 15.

59. The monoclonal antibody of any one of claims 56-58, wherein the BiTE further comprises a heavy chain variable domain (VH) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 16.

60. The monoclonal antibody of any one of claims 34-59, wherein the monoclonal antibody or antigen-binding fragment thereof is a multifunctional antibody.

61. The monoclonal antibody of any one of claims 34-60, wherein the monoclonal antibody or antigen-binding fragment thereof antibody further comprises a conjugated therapeutic moiety.

62. The monoclonal antibody of any one of claims 34-61, wherein the selective binding of the antibody to the complex comprising the HLA-E and the neoantigen induces an immune response in a cell.

63. The monoclonal antibody of claim 62, wherein the immune response comprises activation of T cells.

64. The monoclonal antibody of claim 63, wherein the T cell is a CD8+ T cell.

65. The monoclonal antibody of claim 62, wherein the immune response comprises activation of cytotoxic T cells (CTLs).

66. The monoclonal antibody of claim 62, wherein the cell is a cancer cell.

67. A monoclonal antibody or an antigen-binding fragment thereof, comprising a light chain complementarity determining region (CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 1-3.

68. A monoclonal antibody or an antigen-binding fragment thereof, comprising a light chain complementarity determining region (CDR) having an amino acid sequence at least 90% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 1-3.

69. A monoclonal antibody or an antigen-binding fragment thereof, comprising a light chain complementarity determining region (CDR) having an amino acid sequence at least 95% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 1-3.

70. A monoclonal antibody or an antigen-binding fragment thereof, comprising a light chain complementarity determining region (CDR) having an amino acid sequence at least 99% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 1-3.

71. A monoclonal antibody or an antigen-binding fragment thereof, comprising a light chain complementarity determining region (CDR) having an amino acid sequence 100% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 1-3.

72. The monoclonal antibody of any one of claims 67-71, wherein the monoclonal antibody or antigen-binding fragment thereof comprises a heavy chain complementarity determining region

(CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6.

73. The monoclonal antibody of any one of claims 67-71, wherein the monoclonal antibody or antigen-binding fragment thereof comprises a heavy chain complementarity determining region (CDR) having an amino acid sequence at least 90% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6.

74. The monoclonal antibody of any one of claims 67-71, wherein the monoclonal antibody or antigen-binding fragment thereof comprises a heavy chain complementarity determining region (CDR) having an amino acid sequence at least 95% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6.

75. The monoclonal antibody of any one of claims 67-71, wherein the monoclonal antibody or antigen-binding fragment thereof comprises a heavy chain complementarity determining region (CDR) having an amino acid sequence at least 99% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6.

76. The monoclonal antibody of any one of claims 67-71, wherein the monoclonal antibody or antigen-binding fragment thereof comprises a heavy chain complementarity determining region (CDR) having an amino acid sequence 100% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6.

77. The monoclonal antibody of any one of claims 67-76, wherein the monoclonal antibody or antigen-binding fragment thereof comprises a light chain variable domain (VL) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 7.

78. The monoclonal antibody of any one of claims 67-77, wherein the monoclonal antibody or antigen-binding fragment thereof comprises a heavy chain variable domain (VH) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 8.

79. The monoclonal antibody of any one of claims 67-78, wherein the monoclonal antibody or antigen-binding fragment thereof selectively binds to a complex comprising an HLA-E and a neoantigen.

80. The monoclonal antibody of any one of claims 67-79, wherein the monoclonal antibody or antigen-binding fragment thereof does not have a binding affinity to (i) the HLA-E alone; or (ii) the neoantigen alone.

81. The monoclonal antibody of any one of claims 67-80, wherein the neoantigen is expressed by an antigen processing machinery (APM)-proficient cell.

82. The monoclonal antibody of claim 81, wherein the neoantigen is expressed by a TAP1/2-proficient cell.

83. The monoclonal antibody of any one of claims 67-82, wherein the neoantigen comprises, consists essentially of, or consists of a sequence according to SEQ ID NO: 17 (VMAPRTLIL), SEQ ID NO: 18 (VMAPRTLFL), SEQ ID NO: 19 (VMAPRTLVL), SEQ ID NO: 20 (VTAPRTLLL), SEQ ID NO: 21 (IMAPRTLVL), SEQ ID NO: 23 (VMAPQALLL), SEQ ID NO: 24 (VMAPRALLL), SEQ ID NO: 25 (VMAPRTLLL), SEQ ID NO: 26 (VMAPRTLTL), SEQ ID NO: 27 (VMAPRTVLL), SEQ ID NO: 28 (VMPPTLLL), or SEQ ID NO: 29 (VTAPRTVLL).

84. The monoclonal antibody of any one of claims 67-83, wherein the neoantigen comprises, consists essentially of, or consists of a sequence according to SEQ ID NO: 17 (VMAPRTLIL), SEQ ID NO: 18 (VMAPRTLFL), SEQ ID NO: 19 (VMAPRTLVL), SEQ ID NO: 26 (VMAPRTLTL), or SEQ ID NO: 27 (VMAPRTVLL).

85. The monoclonal antibody of any one of claims 67-84, wherein the HLA-E is HLA-E*0101 or HLA-E*0103.

86. The monoclonal antibody of claim 85, wherein the antibody selectively binds to the complex comprising:

- (a) the HLA-E*0101 and the neoantigen;
- (b) the HLA-E*0103 and the neoantigen; or
- (c) the HLA-E*0101 and the neoantigen, and the HLA-E*0103 and the neoantigen.

87. The monoclonal antibody of any one of claims 67-86, wherein the monoclonal antibody or antigen-binding fragment thereof is a murine antibody, a chimeric antibody, a camelid antibody, a humanized antibody, or a human antibody.

88. The monoclonal antibody of any one of claims 67-87, wherein the monoclonal antibody or antigen-binding fragment thereof is a TCR-like antibody.

89. The monoclonal antibody of any one of claims 67-88, wherein the monoclonal antibody or antigen-binding fragment thereof is a multispecific antibody.

90. The monoclonal antibody of any one of claims 67-89, wherein the monoclonal antibody or antigen-binding fragment thereof is a bispecific antibody.

91. The monoclonal antibody of any one of claims 67-90, wherein the monoclonal antibody or antigen-binding fragment thereof is a bispecific T cell engager (BiTE).

92. The monoclonal antibody of claim 91, wherein the BiTE binds to a CD3 protein associated with a T cell receptor (TCR).

93. The monoclonal antibody of any one of claims 91-92, wherein the BiTE further comprises a light chain complementarity determining region (CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 9-11.

94. The monoclonal antibody of any one of claims 91-93, wherein the BiTE further comprises a heavy chain complementarity determining region (CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 12-14.

95. The monoclonal antibody of any one of claims 91-94, wherein the BiTE further comprises a light chain variable domain (VL) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 15.

96. The monoclonal antibody of any one of claims 91-95, wherein the BiTE further comprises a heavy chain variable domain (VH) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 16.

97. The monoclonal antibody of any one of claims 67-96, wherein the monoclonal antibody or antigen-binding fragment thereof is a multifunctional antibody.

98. The monoclonal antibody of any one of claims 67-97, wherein the monoclonal antibody or antigen-binding fragment thereof antibody further comprises a conjugated therapeutic moiety.

99. The monoclonal antibody of any one of claims 67-98, wherein the selective binding of the antibody to the complex comprising the HLA-E and the neoantigen induces an immune response in a cell.

100. The monoclonal antibody of claim 99, wherein the immune response comprises activation of T cells.

101. The monoclonal antibody of claim 100, wherein the T cell is a CD8+ T cell.

102. The monoclonal antibody of claim 99, wherein the immune response comprises activation of cytotoxic T cells (CTLs).

103. The monoclonal antibody of claim 99, wherein the cell is a cancer cell.

104. A monoclonal antibody or an antigen-binding fragment thereof, comprising a heavy chain complementarity determining region (CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6.

105. A monoclonal antibody or an antigen-binding fragment thereof, comprising a heavy chain complementarity determining region (CDR) having an amino acid sequence at least 90% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6.

106. A monoclonal antibody or an antigen-binding fragment thereof, comprising a heavy chain complementarity determining region (CDR) having an amino acid sequence at least 95% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6.

107. A monoclonal antibody or an antigen-binding fragment thereof, comprising a heavy chain complementarity determining region (CDR) having an amino acid sequence at least 99% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6.

108. A monoclonal antibody or an antigen-binding fragment thereof, comprising a heavy chain complementarity determining region (CDR) having an amino acid sequence 100% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6.

109. The monoclonal antibody of any one of claims 104-108, wherein the monoclonal antibody or antigen-binding fragment comprises a light chain complementarity determining region (CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 1-3.

110. The monoclonal antibody of any one of claims 104-108, wherein the monoclonal antibody or antigen-binding fragment comprises a light chain complementarity determining region (CDR) having an amino acid sequence at least 90% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 1-3.

111. The monoclonal antibody of any one of claims 104-108, wherein the monoclonal antibody or antigen-binding fragment comprises a light chain complementarity determining region

(CDR) having an amino acid sequence at least 95% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 1-3.

112. The monoclonal antibody of any one of claims 104-108, wherein the monoclonal antibody or antigen-binding fragment comprises a light chain complementarity determining region (CDR) having an amino acid sequence at least 99% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 1-3.

113. The monoclonal antibody of any one of claims 104-108, wherein the monoclonal antibody or antigen-binding fragment comprises a light chain complementarity determining region (CDR) having an amino acid sequence 100% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 1-3.

114. The monoclonal antibody of any one of claims 104-113, wherein the monoclonal antibody or antigen-binding fragment thereof comprises a heavy chain variable domain (VH) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 8.

115. The monoclonal antibody of any one of claims 104-114, wherein the monoclonal antibody or antigen-binding fragment thereof comprises a light chain variable domain (VL) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 7.

116. The monoclonal antibody of any one of claims 104-115, wherein the monoclonal antibody or antigen-binding fragment thereof selectively binds to a complex comprising an HLA-E and a neoantigen.

117. The monoclonal antibody of any one of claims 104-116, wherein the monoclonal antibody or antigen-binding fragment thereof does not have a binding affinity to (i) the HLA-E alone; or (ii) the neoantigen alone.

118. The monoclonal antibody of any one of claims 104-117, wherein the neoantigen is expressed by an antigen processing machinery (APM)-proficient cell.

119. The monoclonal antibody of claim 118, wherein the neoantigen is expressed by a TAP1/2-proficient cell.

120. The monoclonal antibody of any one of claims 104-119, wherein the neoantigen comprises, consists essentially of, or consists of a sequence according to SEQ ID NO: 17 (VMAPRTLIL), SEQ ID NO: 18 (VMAPRTLFL), SEQ ID NO: 19 (VMAPRTLVL), SEQ ID NO: 20 (VTAPRTLLL), SEQ ID NO: 21 (IMAPRTLVL), SEQ ID NO: 23 (VMAPQALLL), SEQ ID NO: 24 (VMAPRALLL), SEQ ID NO: 25 (VMAPRTLLL), SEQ ID NO: 26 (VMAPRTLTL), SEQ ID NO: 27 (VMAPRTVLL), SEQ ID NO: 28 (VMPPTLLL), or SEQ ID NO: 29 (VTAPRTVLL).

121. The monoclonal antibody of any one of claims 104-120, wherein the neoantigen comprises, consists essentially of, or consists of a sequence according to SEQ ID NO: 17 (VMAPRTLIL), SEQ ID NO: 18 (VMAPRTLFL), SEQ ID NO: 19 (VMAPRTLVL), SEQ ID NO: 26 (VMAPRTLTL), or SEQ ID NO: 27 (VMAPRTVLL).

122. The monoclonal antibody of any one of claims 104-121, wherein the HLA-E is HLA-E*0101 or HLA-E*0103.

123. The monoclonal antibody of claim 122, wherein the antibody selectively binds to the complex comprising:

- (a) the HLA-E*0101 and the neoantigen;
- (b) the HLA-E*0103 and the neoantigen; or
- (c) the HLA-E*0101 and the neoantigen, and the HLA-E*0103 and the neoantigen.

124. The monoclonal antibody of any one of claims 104-123, wherein the monoclonal antibody or antigen-binding fragment thereof is a murine antibody, a chimeric antibody, a camelid antibody, a humanized antibody, or a human antibody.

125. The monoclonal antibody of any one of claims 104-124, wherein the monoclonal antibody or antigen-binding fragment thereof is a TCR-like antibody.

126. The monoclonal antibody of any one of claims 104-125, wherein the monoclonal antibody or antigen-binding fragment thereof is a multispecific antibody.

127. The monoclonal antibody of any one of claims 104-126, wherein the monoclonal antibody or antigen-binding fragment thereof is a bispecific antibody.

128. The monoclonal antibody of any one of claims 104-127, wherein the monoclonal antibody or antigen-binding fragment thereof is a bispecific T cell engager (BiTE).

129. The monoclonal antibody of claim 128, wherein the BiTE binds to a CD3 protein associated with a T cell receptor (TCR).

130. The monoclonal antibody of any one of claims 128-129, wherein the BiTE further comprises a light chain complementarity determining region (CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 9-11.

131. The monoclonal antibody of any one of claims 128-130, wherein the BiTE further comprises a heavy chain complementarity determining region (CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 12-14.

132. The monoclonal antibody of any one of claims 128-131, wherein the BiTE further comprises a light chain variable domain (VL) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 15.

133. The monoclonal antibody of any one of claims 128-132, wherein the BiTE further comprises a heavy chain variable domain (VH) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 16.

134. The monoclonal antibody of any one of claims 104-133, wherein the monoclonal antibody or antigen-binding fragment thereof is a multifunctional antibody.

135. The monoclonal antibody of any one of claims 104-134, wherein the monoclonal antibody or antigen-binding fragment thereof antibody further comprises a conjugated therapeutic moiety.

136. The monoclonal antibody of any one of claims 104-135, wherein the selective binding of the antibody to the complex comprising the HLA-E and the neoantigen induces an immune response in a cell.

137. The monoclonal antibody of claim 136, wherein the immune response comprises activation of T cells.

138. The monoclonal antibody of claim 137, wherein the T cell is a CD8+ T cell.

139. The monoclonal antibody of claim 136, wherein the immune response comprises activation of cytotoxic T cells (CTLs).

140. The monoclonal antibody of claim 136, wherein the cell is a cancer cell.

141. A bispecific antibody or an antigen-binding fragment thereof, comprising:

(a) a light chain complementarity determining region (CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 1-3; or a heavy chain complementarity determining region (CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6; and

(b) a light chain complementarity determining region (CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 9-11; or a heavy chain complementarity determining region (CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 12-14.

142. The bispecific antibody of claim 141, wherein the bispecific antibody comprises:

(a) a light chain variable domain (VL) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 7; or a heavy chain variable domain (VH) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 8; and

(b) a light chain variable domain (VL) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 15; or a heavy chain variable domain (VH) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 16.

143. A bispecific antibody or an antigen-binding fragment thereof, comprising:

(a) a light chain complementarity determining region (CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 1-3; and a heavy chain complementarity determining region (CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6; and

(b) a light chain complementarity determining region (CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 9-11; and a heavy chain complementarity determining region (CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 12-14.

144. The bispecific antibody of claim 143, wherein the bispecific antibody comprises:
- (a) a light chain variable domain (VL) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 7; and a heavy chain variable domain (VH) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 8; and
 - (b) a light chain variable domain (VL) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 15; and a heavy chain variable domain (VH) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 16.
145. The bispecific antibody of any one of claims 141-144, wherein the bispecific antibody selectively binds to a complex comprising an HLA-E and a neoantigen.
146. The bispecific antibody of any one of claims 141-145, wherein the bispecific antibody does not have a binding affinity to (i) the HLA-E alone; or (ii) the neoantigen alone.
147. The bispecific antibody of any one of claims 141-146, wherein the neoantigen is expressed by an antigen processing machinery (APM)-proficient cell.
148. The bispecific antibody of claim 147, wherein the neoantigen is expressed by a TAP1/2-proficient cell.
149. The bispecific antibody of any one of claims 141-148, wherein the neoantigen comprises, consists essentially of, or consists of a sequence according to SEQ ID NO: 17 (VMAPRTLIL), SEQ ID NO: 18 (VMAPRTLFL), SEQ ID NO: 19 (VMAPRTLVL), SEQ ID NO: 20 (VTAPRTLIL), SEQ ID NO: 21 (IMAPRTLVL), SEQ ID NO: 23 (VMAPQALLL), SEQ ID NO: 24 (VMAPRALLL), SEQ ID NO: 25 (VMAPRTLIL), SEQ ID NO: 26 (VMAPRTLTL), SEQ ID NO: 27 (VMAPRTVLL), SEQ ID NO: 28 (VMPRTLIL), or SEQ ID NO: 29 (VTAPRTVLL).
150. The bispecific antibody of any one of claims 141-149, wherein the neoantigen comprises, consists essentially of, or consists of a sequence according to SEQ ID NO: 17 (VMAPRTLIL), SEQ ID NO: 18 (VMAPRTLFL), SEQ ID NO: 19 (VMAPRTLVL), SEQ ID NO: 26 (VMAPRTLTL), or SEQ ID NO: 27 (VMAPRTVLL).
151. The bispecific antibody of any one of claims 141-150, wherein the HLA-E is HLA-E*0101 or HLA-E*0103.

152. The bispecific antibody of claim 151, wherein the antibody selectively binds to the complex comprising:

- (a) the HLA-E*0101 and the neoantigen;
- (b) the HLA-E*0103 and the neoantigen; or
- (c) the HLA-E*0101 and the neoantigen, and the HLA-E*0103 and the neoantigen.

153. The bispecific antibody of any one of claims 141-152, wherein the monoclonal antibody or antigen-binding fragment thereof is a murine antibody, a chimeric antibody, a camelid antibody, a humanized antibody, or a human antibody.

154. The bispecific antibody of any one of claims 104-153, wherein the monoclonal antibody or antigen-binding fragment thereof is a bispecific T cell engager (BiTE).

155. The bispecific antibody of claim 154, wherein the BiTE binds to a CD3 protein associated with a T cell receptor (TCR).

156. The bispecific antibody of any one of claims 141-155, wherein the monoclonal antibody or antigen-binding fragment thereof is a multifunctional antibody.

157. The bispecific antibody of any one of claims 141-156, wherein the monoclonal antibody or antigen-binding fragment thereof antibody further comprises a conjugated therapeutic moiety.

158. The bispecific antibody of any one of claims 141-157, wherein the selective binding of the antibody to the complex comprising the HLA-E and the neoantigen induces an immune response in a cell.

159. The bispecific antibody of claim 158, wherein the immune response comprises activation of T cells.

160. The bispecific antibody of claim 159, wherein the T cell is a CD8+ T cell.

161. The bispecific antibody of claim 158, wherein the immune response comprises activation of cytotoxic T cells (CTLs).

162. The bispecific antibody of claim 158, wherein the cell is a cancer cell.

163. A pharmaceutical composition comprising: (a) a monoclonal antibody or an antigen-binding fragment thereof according to any one of claims 1-140, or a bispecific antibody or an

antigen-binding fragment thereof according to any one of claims 141-162; and (b) a pharmaceutically acceptable carrier or excipient.

164. A method of treating cancer in an individual in need thereof, comprising administering to the individual an effective amount of a monoclonal antibody or an antigen-binding fragment thereof comprising a light chain complementarity determining region (CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 1-3.

165. A method of treating cancer in an individual in need thereof, comprising administering to the individual an effective amount of a monoclonal antibody or an antigen-binding fragment thereof comprising a heavy chain complementarity determining region (CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6.

166. The method of claim 164 or claim 165, wherein the monoclonal antibody or antigen-binding fragment thereof comprises (a) a light chain complementarity determining region (CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 1-3; and (b) a heavy chain complementarity determining region (CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6.

167. The method of any one of claims 164-166, wherein the monoclonal antibody or antigen-binding fragment thereof comprises (a) a light chain complementarity determining region (CDR) having an amino acid sequence at least 90% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 1-3; and (b) a heavy chain complementarity determining region (CDR) having an amino acid sequence at least 90% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6.

168. The method of any one of claims 164-167, wherein the monoclonal antibody or antigen-binding fragment thereof comprises (a) a light chain complementarity determining region (CDR) having an amino acid sequence at least 95% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 1-3; and (b) a heavy chain complementarity determining region (CDR) having an amino acid sequence at least 95% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6.

169. The method of any one of claims 164-168, wherein the monoclonal antibody or antigen-binding fragment thereof comprises (a) a light chain complementarity determining region (CDR) having an amino acid sequence at least 99% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 1-3; and (b) a heavy chain complementarity determining region (CDR) having an amino acid sequence at least 99% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6.

170. The method of any one of claims 164-169, wherein the monoclonal antibody or antigen-binding fragment thereof comprises (a) a light chain complementarity determining region (CDR) having an amino acid sequence 100% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 1-3; and (b) a heavy chain complementarity determining region (CDR) having an amino acid sequence 100% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6.

171. The method of any one of claims 164-170, wherein the monoclonal antibody or antigen-binding fragment thereof comprises a light chain variable domain (VL) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 7.

172. The method of any one of claims 164-171, wherein the monoclonal antibody or antigen-binding fragment thereof comprises a heavy chain variable domain (VH) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 8.

173. The method of any one of claims 164-172, wherein the monoclonal antibody or antigen-binding fragment thereof selectively binds to a complex comprising an HLA-E and a neoantigen.

174. The method of any one of claims 164-173, wherein the monoclonal antibody or antigen-binding fragment thereof does not have a binding affinity to (i) the HLA-E alone; or (ii) the neoantigen alone.

175. The method of any one of claims 164-174, wherein the neoantigen is expressed by an antigen processing machinery (APM)-proficient cell.

176. The method of claim 175, wherein the neoantigen is expressed by a TAP1/2-proficient cell.

177. The method of any one of claims 164-176, wherein the neoantigen comprises, consists essentially of, or consists of a sequence according to SEQ ID NO: 17 (VMAPRTLIL), SEQ

ID NO: 18 (VMAPRTLFL), SEQ ID NO: 19 (VMAPRTLVL), SEQ ID NO: 20 (VTAPRTLLL), SEQ ID NO: 21 (IMAPRTLVL), SEQ ID NO: 23 (VMAPQALLL), SEQ ID NO: 24 (VMAPRALLL), SEQ ID NO: 25 (VMAPRTLLL), SEQ ID NO: 26 (VMAPRTLTL), SEQ ID NO: 27 (VMAPRTVLL), SEQ ID NO: 28 (VMPPTLLL), or SEQ ID NO: 29 (VTAPRTVLL).

178. The method of any one of claims 164-177, wherein the neoantigen comprises, consists essentially of, or consists of a sequence according to SEQ ID NO: 17 (VMAPRTLIL), SEQ ID NO: 18 (VMAPRTLFL), SEQ ID NO: 19 (VMAPRTLVL), SEQ ID NO: 26 (VMAPRTLTL), or SEQ ID NO: 27 (VMAPRTVLL).

179. The method of any one of claims 164-178, wherein the HLA-E is HLA-E*0101 or HLA-E*0103.

180. The method of claim 179, wherein the antibody selectively binds to the complex comprising:

- (a) the HLA-E*0101 and the neoantigen;
- (b) the HLA-E*0103 and the neoantigen; or
- (c) the HLA-E*0101 and the neoantigen, and the HLA-E*0103 and the neoantigen.

181. The method of any one of claims 164-180, wherein the monoclonal antibody or antigen-binding fragment thereof is a murine antibody, a chimeric antibody, a camelid antibody, a humanized antibody, or a human antibody.

182. The method of any one of claims 164-181, wherein the monoclonal antibody or antigen-binding fragment thereof is a TCR-like antibody.

183. The method of any one of claims 164-182, wherein the monoclonal antibody or antigen-binding fragment thereof is a multispecific antibody.

184. The method of any one of claims 164-183, wherein the monoclonal antibody or antigen-binding fragment thereof is a bispecific antibody.

185. The method of any one of claims 164-184, wherein the monoclonal antibody or antigen-binding fragment thereof is a bispecific T cell engager (BiTE).

186. The method of claim 185, wherein the BiTE binds to a CD3 protein associated with a T cell receptor (TCR).

187. The method of any one of claims 185-186, wherein the BiTE further comprises a light chain complementarity determining region (CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 9-11.

188. The method of any one of claims 185-187, wherein the BiTE further comprises a heavy chain complementarity determining region (CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 12-14.

189. The method of any one of claims 185-188, wherein the BiTE further comprises a light chain variable domain (VL) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 15.

190. The method of any one of claims 185-189, wherein the BiTE further comprises a heavy chain variable domain (VH) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 16.

191. The method of any one of claims 164-190, wherein the monoclonal antibody or antigen-binding fragment thereof is a multifunctional antibody.

192. The method of any one of claims 164-191, wherein the monoclonal antibody or antigen-binding fragment thereof antibody further comprises a conjugated therapeutic moiety.

193. The method of any one of claims 164-192, wherein the selective binding of the antibody to the complex comprising the HLA-E and the neoantigen induces an immune response in a cell.

194. The method of claim 193, wherein the immune response comprises activation of T cells.

195. The method of claim 194, wherein the T cell is a CD8+ T cell.

196. The method of claim 193, wherein the immune response comprises activation of cytotoxic T cells (CTLs).

197. The method of any one of claims 164-193, wherein the cancer is breast cancer, kidney cancer, lung cancer, ovarian cancer, colorectal cancer, pancreatic cancer, choriocarcinoma, non-small cell lung carcinoma (NSCLC), gastric cancer, cervical cancer, or head and neck cancer.

198. The method of any one of claims 164-193, wherein the cancer is a leukemia, a lymphoma or a myeloma.

199. The method of any one of claims 164-193, wherein the cancer is multiple myeloma (MM), acute myeloid leukemia (AML), or myelodysplastic syndrome.

200. The method of any one of claims 164-193, wherein the cancer is a B-cell malignancy.

201. The method of any one of claims 164-193, wherein the cancer is mantle cell lymphoma.

202. A method of treating cancer in an individual in need thereof, comprising administering to the individual an effective amount of a bispecific antibody or an antigen-binding fragment thereof, comprising:

(a) a light chain complementarity determining region (CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 1-3; or a heavy chain complementarity determining region (CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6; and

(b) a light chain complementarity determining region (CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 9-11; or a heavy chain complementarity determining region (CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 12-14.

203. The method of claim 201, wherein the bispecific antibody comprises:

(a) a light chain variable domain (VL) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 7; or a heavy chain variable domain (VH) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 8; and

(b) a light chain variable domain (VL) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 15; or a heavy chain variable domain (VH) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 16.

204. A method of treating cancer in an individual in need thereof, comprising administering to the individual an effective amount of a bispecific antibody or an antigen-binding fragment thereof, comprising:

(a) a light chain complementarity determining region (CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 1-3; and a heavy chain complementarity determining region (CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6; and

(b) a light chain complementarity determining region (CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 9-11; and a heavy chain complementarity determining region (CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 12-14.

205. The method of claim 204, wherein the bispecific antibody comprises:

(a) a light chain variable domain (VL) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 7; and a heavy chain variable domain (VH) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 8; and

(b) a light chain variable domain (VL) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 15; and a heavy chain variable domain (VH) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 16.

206. The method of any one of claims 201-205, wherein the bispecific antibody or antigen-binding fragment thereof selectively binds to a complex comprising an HLA-E and a neoantigen.

207. The method of any one of claims 201-206, wherein the bispecific antibody or antigen-binding fragment thereof does not have a binding affinity to (i) the HLA-E alone; or (ii) the neoantigen alone.

208. The method of any one of claims 201-207, wherein the neoantigen is expressed by an antigen processing machinery (APM)-proficient cell.

209. The method of claim 208, wherein the neoantigen is expressed by a TAP1/2-proficient cell.

210. The method of any one of claims 201-209, wherein the neoantigen comprises, consists essentially of, or consists of a sequence according to SEQ ID NO: 17 (VMAPRTLIL), SEQ

ID NO: 18 (VMAPRTLFL), SEQ ID NO: 19 (VMAPRTLVL), SEQ ID NO: 20 (VTAPRTLLL), SEQ ID NO: 21 (IMAPRTLVL), SEQ ID NO: 23 (VMAPQALLL), SEQ ID NO: 24 (VMAPRALLL), SEQ ID NO: 25 (VMAPRTLLL), SEQ ID NO: 26 (VMAPRTLTL), SEQ ID NO: 27 (VMAPRTVLL), SEQ ID NO: 28 (VMPRTLLL), or SEQ ID NO: 29 (VTAPRTVLL).

211. The method of any one of claims 201-210, wherein the neoantigen comprises, consists essentially of, or consists of a sequence according to SEQ ID NO: 17 (VMAPRTLIL), SEQ ID NO: 18 (VMAPRTLFL), SEQ ID NO: 19 (VMAPRTLVL), SEQ ID NO: 26 (VMAPRTLTL), or SEQ ID NO: 27 (VMAPRTVLL).

212. The method of any one of claims 201-211, wherein the HLA-E is HLA-E*0101 or HLA-E*0103.

213. The method of claim 212, wherein the bispecific antibody selectively binds to the complex comprising:

- (a) the HLA-E*0101 and the neoantigen;
- (b) the HLA-E*0103 and the neoantigen; or
- (c) the HLA-E*0101 and the neoantigen, and the HLA-E*0103 and the neoantigen.

214. The method of any one of claims 201-213, wherein the bispecific antibody or antigen-binding fragment thereof is a murine antibody, a chimeric antibody, a camelid antibody, a humanized antibody, or a human antibody.

215. The method of any one of claims 201-214, wherein the bispecific antibody or antigen-binding fragment thereof is a TCR-like antibody.

216. The method of any one of claims 201-215, wherein the bispecific antibody or antigen-binding fragment thereof is a bispecific T cell engager (BiTE).

217. The method of claim 216, wherein the BiTE binds to a CD3 protein associated with a T cell receptor (TCR).

218. The method of any one of claims 201-217, wherein the bispecific antibody or antigen-binding fragment thereof is a multifunctional antibody.

219. The method of any one of claims 201-218, wherein the bispecific antibody or antigen-binding fragment thereof antibody further comprises a conjugated therapeutic moiety.

220. The method of any one of claims 201-219, wherein the selective binding of the antibody to the complex comprising the HLA-E and the neoantigen induces an immune response in a cell.
221. The method of claim 220, wherein the immune response comprises activation of T cells.
222. The method of claim 221, wherein the T cell is a CD8+ T cell.
223. The method of claim 220, wherein the immune response comprises activation of cytotoxic T cells (CTLs).
224. The method of any one of claims 201-223, wherein the bispecific antibody is administered at a therapeutically effective amount.
225. The method of any one of claims 201-224, wherein the cancer is breast cancer, kidney cancer, lung cancer, ovarian cancer, colorectal cancer, pancreatic cancer, choriocarcinoma, non-small cell lung carcinoma (NSCLC), gastric cancer, cervical cancer, or head and neck cancer.
226. The method of any one of claims 201-224, wherein the cancer is a leukemia, a lymphoma or a myeloma.
227. The method of any one of claims 201-224, wherein the cancer is multiple myeloma (MM), acute myeloid leukemia (AML), or myelodysplastic syndrome.
228. The method of any one of claims 201-224, wherein the cancer is a B-cell malignancy.
229. The method of any one of claims 201-224, wherein the cancer is mantle cell lymphoma.
230. A monoclonal antibody or an antigen-binding fragment thereof, comprising a light chain (LC) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 31.

231. A monoclonal antibody or an antigen-binding fragment thereof, comprising a light chain (LC) comprising an amino acid sequence at least 90% identical to an amino acid sequence set forth as SEQ ID NO: 31.

232. A monoclonal antibody or an antigen-binding fragment thereof, comprising a light chain (LC) comprising an amino acid sequence at least 95% identical to an amino acid sequence set forth as SEQ ID NO:31.

233. A monoclonal antibody or an antigen-binding fragment thereof, comprising a light chain (LC) comprising an amino acid sequence at least 99% identical to an amino acid sequence set forth as SEQ ID NO: 31.

234. A monoclonal antibody or an antigen-binding fragment thereof, comprising a light chain (LC) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 31.

235. The monoclonal antibody of any one of claims 230-234, wherein the monoclonal antibody or antigen-binding fragment thereof comprises a heavy chain (HC) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 30.

236. The monoclonal antibody of any one of claims 230-234, wherein the monoclonal antibody or antigen-binding fragment thereof comprises a heavy chain (HC) comprising an amino acid sequence at least 90% identical to an amino acid sequence set forth as SEQ ID NO: 30.

237. The monoclonal antibody of any one of claims 230-234, wherein the monoclonal antibody or antigen-binding fragment thereof comprises a heavy chain (HC) comprising an amino acid sequence at least 95% identical to an amino acid sequence set forth as SEQ ID NO: 30.

238. The monoclonal antibody of any one of claims 230-234, wherein the monoclonal antibody or antigen-binding fragment thereof comprises a heavy chain (HC) comprising an amino acid sequence at least 99% identical to an amino acid sequence set forth as SEQ ID NO: 30.

239. The monoclonal antibody of any one of claims 230-234, wherein the monoclonal antibody or antigen-binding fragment thereof comprises a heavy chain (HC) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 30.

240. The monoclonal antibody of any one of claims 230-234, wherein the monoclonal antibody or antigen-binding fragment thereof comprises a heavy chain (HC) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 32.

241. The monoclonal antibody of any one of claims 230-234, wherein the monoclonal antibody or antigen-binding fragment thereof comprises a heavy chain (HC) comprising an amino acid sequence at least 90% identical to an amino acid sequence set forth as SEQ ID NO: 32.

242. The monoclonal antibody of any one of claims 230-234, wherein the monoclonal antibody or antigen-binding fragment thereof comprises a heavy chain (HC) comprising an amino acid sequence at least 95% identical to an amino acid sequence set forth as SEQ ID NO: 32.

243. The monoclonal antibody of any one of claims 230-234, wherein the monoclonal antibody or antigen-binding fragment thereof comprises a heavy chain (HC) comprising an amino acid sequence at least 99% identical to an amino acid sequence set forth as SEQ ID NO: 32.

244. The monoclonal antibody of any one of claims 230-234, wherein the monoclonal antibody or antigen-binding fragment thereof comprises a heavy chain (HC) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 32.

245. The monoclonal antibody of any one of claims 230-234, wherein the monoclonal antibody or antigen-binding fragment thereof comprises a heavy chain (HC) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 33.

246. The monoclonal antibody of any one of claims 230-234, wherein the monoclonal antibody or antigen-binding fragment thereof comprises a heavy chain (HC) comprising an amino acid sequence at least 90% identical to an amino acid sequence set forth as SEQ ID NO: 33.

247. The monoclonal antibody of any one of claims 230-234, wherein the monoclonal antibody or antigen-binding fragment thereof comprises a heavy chain (HC) comprising an amino acid sequence at least 95% identical to an amino acid sequence set forth as SEQ ID NO: 33.

248. The monoclonal antibody of any one of claims 230-234, wherein the monoclonal antibody or antigen-binding fragment thereof comprises a heavy chain (HC) comprising an amino acid sequence at least 99% identical to an amino acid sequence set forth as SEQ ID NO: 33.

249. The monoclonal antibody of any one of claims 230-234, wherein the monoclonal antibody or antigen-binding fragment thereof comprises a heavy chain (HC) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 33.

250. A monoclonal antibody or an antigen-binding fragment thereof, comprising a light chain (LC) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 35.

251. A monoclonal antibody or an antigen-binding fragment thereof, comprising a light chain (LC) comprising an amino acid sequence at least 90% identical to an amino acid sequence set forth as SEQ ID NO: 35.

252. A monoclonal antibody or an antigen-binding fragment thereof, comprising a light chain (LC) comprising an amino acid sequence at least 95% identical to an amino acid sequence set forth as SEQ ID NO: 35.

253. A monoclonal antibody or an antigen-binding fragment thereof, comprising a light chain (LC) comprising an amino acid sequence at least 99% identical to an amino acid sequence set forth as SEQ ID NO: 35.

254. A monoclonal antibody or an antigen-binding fragment thereof, comprising a light chain (LC) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 35.

255. The monoclonal antibody of any one of claims 250-254, wherein the monoclonal antibody or antigen-binding fragment thereof comprises a heavy chain (HC) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 34.

256. The monoclonal antibody of any one of claims 250-254, wherein the monoclonal antibody or antigen-binding fragment thereof comprises a heavy chain (HC) comprising an amino acid sequence at least 90% identical to an amino acid sequence set forth as SEQ ID NO: 34.

257. The monoclonal antibody of any one of claims 250-254, wherein the monoclonal antibody or antigen-binding fragment thereof comprises a heavy chain (HC) comprising an amino acid sequence at least 95% identical to an amino acid sequence set forth as SEQ ID NO: 34.

258. The monoclonal antibody of any one of claims 250-254, wherein the monoclonal antibody or antigen-binding fragment thereof comprises a heavy chain (HC) comprising an amino acid sequence at least 99% identical to an amino acid sequence set forth as SEQ ID NO: 34.

259. The monoclonal antibody of any one of claims 250-254, wherein the monoclonal antibody or antigen-binding fragment thereof comprises a heavy chain (HC) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 34.

260. The monoclonal antibody of any one of claims 230-259, wherein the monoclonal antibody or antigen-binding fragment thereof selectively binds to a complex comprising an HLA-E and a neoantigen.

261. The monoclonal antibody of any one of claims 230-260, wherein the monoclonal antibody or antigen-binding fragment thereof does not have a binding affinity to (i) the HLA-E alone; or (ii) the neoantigen alone.

262. The monoclonal antibody of any one of claims 230-261, wherein the neoantigen is expressed by an antigen processing machinery (APM)-proficient cell.

263. The monoclonal antibody of claim 262, wherein the neoantigen is expressed by a TAP1/2-proficient cell.

264. The monoclonal antibody of any one of claims 230-263, wherein the neoantigen comprises, consists essentially of, or consists of a sequence according to SEQ ID NO: 17 (VMAPRTLIL), SEQ ID NO: 18 (VMAPRTLFL), SEQ ID NO: 19 (VMAPRTLVL), SEQ ID NO: 20 (VTAPRTLIL), SEQ ID NO: 21 (IMAPRTLVL), SEQ ID NO: 23 (VMAQALLL), SEQ ID NO: 24 (VMAPRALLL), SEQ ID NO: 25 (VMAPRTLIL), SEQ ID NO: 26 (VMAPRTLTL), SEQ ID NO: 27 (VMAPRTVLL), SEQ ID NO: 28 (VMPRTLIL), or SEQ ID NO: 29 (VTAPRTLIL).

265. The monoclonal antibody of any one of claims 230-264, wherein the neoantigen comprises, consists essentially of, or consists of a sequence according to SEQ ID NO: 17 (VMAPRTLIL), SEQ ID NO: 18 (VMAPRTLFL), SEQ ID NO: 19 (VMAPRTLVL), SEQ ID NO: 26 (VMAPRTLTL), or SEQ ID NO: 27 (VMAPRTVLL).

266. The monoclonal antibody of any one of claims 230-265, wherein the HLA-E is HLA-E*0101 or HLA-E*0103.

267. The monoclonal antibody of claim 266, wherein the antibody selectively binds to the complex comprising:

- (a) the HLA-E*0101 and the neoantigen;
- (b) the HLA-E*0103 and the neoantigen; or
- (c) the HLA-E*0101 and the neoantigen, and the HLA-E*0103 and the neoantigen.

268. The monoclonal antibody of any one of claims 230-267, wherein the monoclonal antibody or antigen-binding fragment thereof is a murine antibody, a chimeric antibody, a camelid antibody, a humanized antibody, or a human antibody.

269. The monoclonal antibody of any one of claims 230-268, wherein the monoclonal antibody or antigen-binding fragment thereof is a TCR-like antibody.

270. The monoclonal antibody of any one of claims 230-269, wherein the monoclonal antibody or antigen-binding fragment thereof is a multispecific antibody.

271. The monoclonal antibody of any one of claims 230-270, wherein the monoclonal antibody or antigen-binding fragment thereof is a bispecific antibody.

272. The monoclonal antibody of any one of claims 230-271, wherein the monoclonal antibody or antigen-binding fragment thereof is a bispecific T cell engager (BiTE).

273. The monoclonal antibody of claim 272, wherein the BiTE binds to a CD3 protein associated with a T cell receptor (TCR).

274. The monoclonal antibody of any one of claims 272-273, wherein the BiTE further comprises a light chain variable domain (VL) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 15.

275. The monoclonal antibody of any one of claims 272-273, wherein the BiTE further comprises a heavy chain variable domain (VH) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 16.

276. The monoclonal antibody of any one of claims 230-275, wherein the monoclonal antibody or antigen-binding fragment thereof is a multifunctional antibody.

277. The monoclonal antibody of any one of claims 230-276, wherein the monoclonal antibody or antigen-binding fragment thereof antibody further comprises a conjugated therapeutic moiety.

278. The monoclonal antibody of any one of claims 230-277, wherein the selective binding of the antibody to the complex comprising the HLA-E and the neoantigen induces an immune response in a cell.

279. The monoclonal antibody of claim 278, wherein the immune response comprises activation of T cells.

280. The monoclonal antibody of claim 279, wherein the T cell is a CD8+ T cell.

281. The monoclonal antibody of claim 280, wherein the immune response comprises activation of cytotoxic T cells (CTLs).

282. The monoclonal antibody of claim 281, wherein the cell is a cancer cell.