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(54) **Titre : ANTICORPS ANTI-GLYCO-LAMP1 ET LEURS UTILISATIONS**
(54) **Title: ANTI-GLYCO-LAMP1 ANTIBODIES AND THEIR USES**

Overlay of Mouse mAbs on T47D COSMC-KO Cells

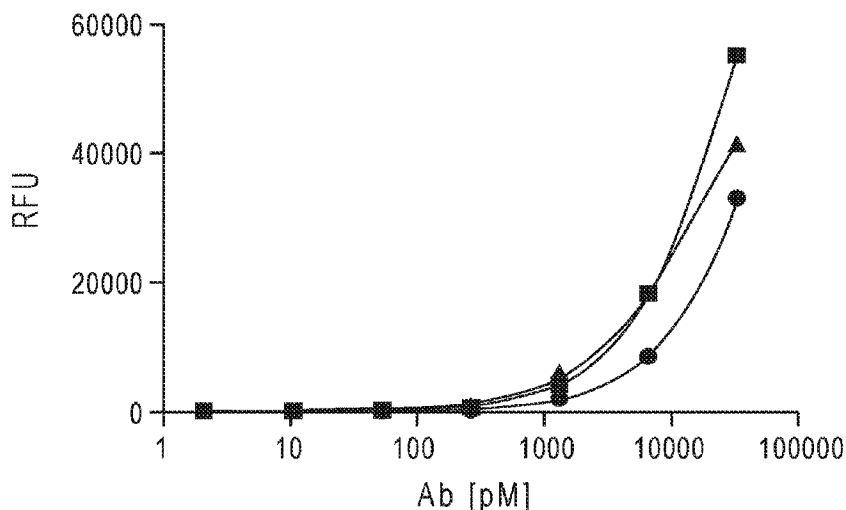


FIG. 1B-1

(57) **Abrégé/Abstract:**

The present disclosure relates to anti-glyco-LAMP1 antibodies and antigen binding fragments thereof that specifically bind to a cancer-specific glycosylation variant of LAMP1 and related fusion proteins and antibody-drug conjugates, as well as nucleic acids encoding such biomolecules. The present disclosure further relates to use of the antibodies, antigen-binding fragments, fusion proteins, antibody-drug conjugates and nucleic acids for cancer therapy.

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Overlay of Mouse mAbs on T47D COSMC-KO Cells

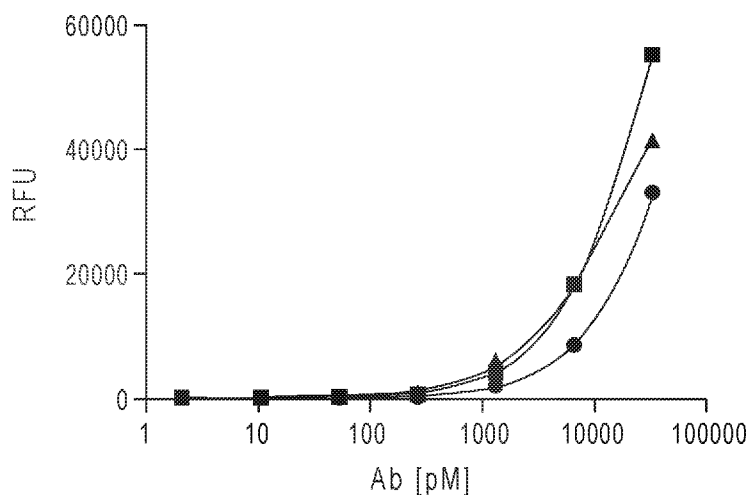


FIG. 1B-1

(57) Abstract: The present disclosure relates to anti-glyco-LAMP1 antibodies and antigen binding fragments thereof that specifically bind to a cancer-specific glycosylation variant of LAMP1 and related fusion proteins and antibody-drug conjugates, as well as nucleic acids encoding such biomolecules. The present disclosure further relates to use of the antibodies, antigen-binding fragments, fusion proteins, antibody-drug conjugates and nucleic acids for cancer therapy.

[Continued on next page]



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ANTI-GLYCO-LAMP1 ANTIBODIES AND THEIR USES

1. CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims the priority benefit of U.S. provisional application no. 63/240,773, filed September 3, 2021, the contents of which are incorporated herein in their entireties by reference thereto.

2. BACKGROUND

[0002] Therapies redirecting T cell responses using chimeric antigen receptors (CARs) have emerged as a potent tool in cancer immunotherapies and have proved highly effective in haematological cancers, targeting antigens shared with nonessential tissues such as CD19 in B cell malignancies (Brentjens *et al.*, 2013, *Sci Transl Med.* 5(177):177ra38-177ra38; Grupp *et al.*, 2013, *N Engl J Med.* 368(16):1509–1518; Kalos *et al.*, 2011, *Sci Transl Med.* 3(95):95ra73-95ra73; Kochenderfer *et al.*, 2010, *Blood.* 116(20):4099–4102; Porter *et al.*, 2011, *N Engl J Med.* 365(8):725–733). However, adopting CAR therapies to solid tumours has been challenging because the majority of CAR targets are normal self-antigens overexpressed in solid cancers. As such, adverse effects due to cross-reactions with essential healthy tissues are often reported in studies targeting solid tumours with CAR T cells (Bin Hou *et al.*, 2019, *Dis Markers*, Article ID 3425291). To overcome the challenges of adopting CAR therapies to solid tumours, new cancer-specific antigens allowing selective targeting are required.

[0003] Many cancers express aberrantly glycosylated proteins that are distinct from healthy tissues. Such aberrantly glycosylated proteins contain glycopeptide epitopes that may be suitable for immunotherapy of solid tumors, but only few such glycopeptide epitopes have been identified.

[0004] Lysosome associated membrane protein-1 (LAMP1) is a heavily glycosylated lysosomal membrane protein involved in protecting the lysosomal membrane from intracellular proteolysis (Kundra and Kornfeld, 1999, *J Biol Chem.* 274:31039-31046; Saftig and Klumperman, 2009, *Nat Rev Mol Cell Bio.* 10:623-635). Although LAMP1 is primarily expressed in the endosome-lysosomal membrane of cells, it is also expressed in the plasma membrane (Parkinson-Lawrence *et al.*, 2005, *Cell Immunol.* 236:161-166; Kannan *et al.*, 1996, *Cell Immunol.* 171:10-19). Elevated LAMP1 expression at the cell surface has also been detected in metastatic tumor cells (Kannan *et al.*, *supra*; Adrejewski *et al.*, 1999, *J Biol Chem.* 274:12692-12701; Sarafian *et al.*, 1998, *Int J Cancer.* 75:105-111), with high LAMP1 expression in colorectal neoplasm compared with normal mucosa (Furuta *et al.*, 2001, *Am J Pathol.* 159:449-455). Surface expression of LAMP1 has also been observed in other human cancers, including human fibrosarcoma, colon adenocarcinoma, melanoma, pancreatic adenocarcinoma, and astrocytoma (Sarafin *et al.*, *supra*; Jensen *et al.*, 2013, *Int J Clin Exp Pathol.* 6(7):1294-1305;

Kunzli *et al.*, 2002, *Cancer*. 94(1):228-239). Several monoclonal antibodies that have displayed promising results in tumors with high surface LAMP1 levels (see, e.g., Baudat *et al.*, 2016, *Cancer Res.* 76(14 Supplement):1198), but most of these are not suitably for immunotherapeutic targeting with cytotoxic strategies due to the prominent expression of LAMP1 in healthy tissue. Thus, there is a need for identification of glyco-LAMP1 epitopes that are overexpressed in cancer cells and new therapeutic modalities, such as antibodies and CARs, which target such glyco-LAMP1 epitopes.

3. SUMMARY

[0005] The disclosure captures the tumor specificity of glycopeptide variants by providing therapeutic and diagnostic agents based on antibodies and antigen binding fragments that are selective for cancer-specific epitopes of glyco-LAMP1. The antibodies and antigen-binding fragments advantageously bind to both the LAMP1 backbone and its cancer specific O-linked glycans but not LAMP1 on healthy tissues.

[0006] Accordingly, the present disclosure provides anti-glyco-LAMP1 antibodies and antigen binding fragments thereof that bind to a cancer-specific glycosylation variant of LAMP1. The present disclosure further provides fusion proteins and antibody-drug conjugates comprising anti-glyco-LAMP1 antibodies and antigen binding fragments, and nucleic acids encoding the anti-glyco-LAMP1 antibodies, antigen binding fragments and fusion proteins.

[0007] The present disclosure further provides methods of using the anti-glyco-LAMP1 antibodies, antigen-binding fragments, fusion proteins, antibody-drug conjugates and nucleic acids for cancer therapy.

[0008] In certain aspects, the disclosure provides bispecific and other multispecific anti-glyco-LAMP1 antibodies and antigen binding fragments that bind to a cancer-specific glycosylation variant of LAMP1 and to a second epitope, and fragments and variants thereof. The second epitope can either be on LAMP1 itself, on another protein co-expressed on cancer cells with LAMP1, or on another protein presented on a different cell, such as an activated T cell. Further, also disclosed are nucleic acids encoding such antibodies, including nucleic acids comprising codon-optimized coding regions and nucleic acids comprising coding regions that are not codon-optimized for expression in a particular host cell.

[0009] The anti-glyco-LAMP1 antibodies and binding fragments can be in the form of fusion proteins containing a fusion partner. The fusion partner can be useful to provide a second function, such as a signaling function of the signaling domain of a T cell signaling protein, a peptide modulator of T cell activation or an enzymatic component of a labeling system. Exemplary T cell signaling proteins include 4-1BB, CD28, CD2, and fusion peptides, e.g., CD28-CD3-zeta, 4-1BB-CD3-zeta, CD2-CD3-zeta, CD28-CD2-CD3-zeta, and 4-1BB-CD2-CD3-zeta. 4-1BB, also known as CD137, is a co-stimulatory receptor of T cells; CD2 is a co-

stimulatory receptor of T and NK cells; CD3-zeta is a signal-transduction component of the T-cell antigen receptor. The moiety providing a second function can be a modulator of T cell activation, such as IL-15, IL-15R α , or an IL-15/IL-15R α fusion, can be an MHC-class I-chain-related (MIC) protein domain useful for making a MicAbody, or it can encode a label or an enzymatic component of a labeling system useful in monitoring the extent and/or location of binding *in vivo* or *in vitro*. Constructs encoding these prophylactically and therapeutically active biomolecules placed in the context of T cells, such as autologous T cells, provide a powerful platform for recruiting adoptively transferred T cells to prevent or treat a variety of cancers in some embodiments of the disclosure.

[0010] In certain aspects, an anti-glyco-LAMP1 antibody or antigen-binding fragment of the disclosure comprises heavy and/or light chain CDR sequences (as defined by Kabat, Chothia, IMGT or their combined region of overlap) of the anti-glyco-LAMP1 antibodies 3C7.2C11.1C9 (sometimes referred to herein as “3C7”), 13C3.1C8.1C9 (sometimes referred to herein as “13C3”), or 13G2.1A10.2G5 (sometimes referred to herein as “13G2”) or humanized counterparts thereof. In some embodiments, an anti-glyco-LAMP1 antibody or antigen-binding fragment of the disclosure comprises heavy and/or light chain variable sequences (or encoded by the nucleotide sequences) of the anti-glyco-LAMP1 antibodies 3C7, 13C3, or 13G2 of humanized counterparts thereof. The CDR and variable sequences (as well as their coding sequences) of the anti-glyco-LAMP1 antibodies 3C7, 13C3, and 13G2 are set forth in Tables 1A through 1C, respectively. For clarity, when the term “anti-glyco-LAMP1 antibody” is used in this document, it is intended to include monospecific and multi-specific (including bispecific) anti-glyco-LAMP1 antibodies, antigen-binding fragments of the monospecific and multi-specific antibodies, and fusion proteins and conjugates containing the antibodies and their antigen-binding fragments, unless the context dictates otherwise. Likewise, when the term “anti-glyco-LAMP1 antibody or antigen-binding fragment” is used, it is also intended to include monospecific and multi-specific (including bispecific) anti-glyco-LAMP1 antibodies and their antigen-binding fragments, together with fusion proteins and conjugates containing such antibodies and antigen-binding fragments, unless the context dictates otherwise.

[0011] In other aspects, an anti-glyco-LAMP1 antibody or antigen-binding fragment of the disclosure comprises heavy and/or light chain CDR sequences (or encoded by the nucleotide sequences) set forth in Tables 1A-3D. The CDR sequences set forth in Tables 1A-1C include CDR sequences defined according to the IMGT (Lefranc *et al.*, 2003, *Dev Comparat Immunol* 27:55-77), Kabat (Kabat *et al.*, 1991, *Sequences of Proteins of Immunological Interest*, 5th Ed. Public Health Service, National Institutes of Health, Bethesda, Md.), and Chothia (Al-Lazikani *et al.*, 1997, *J. Mol. Biol* 273:927-948) schemes for defining CDR boundaries. The CDR sequences set forth in Tables 1D-1F are consensus sequences derived from the CDR sequences set forth in Tables 1A through 1C according to the IMGT, Kabat, and Chothia

definitions, respectively. The CDR sequences set forth in Tables 2A through 2C are the combined regions of overlap for the CDR sequences set forth in Tables 1A through 1C, respectively, with the IMGT, Kabat and Chothia sequences shown in underlined bold text. The CDR sequences set forth in Table 2D are the combined regions of overlap for the consensus CDR sequences set forth in Tables 2A-2C. The CDR sequences set forth in Tables 3A-3C are the common regions of overlap for the CDR sequences shown in Tables 1A-1C, respectively. The CDR sequences set forth in Table 3D are the common regions of overlap for the CDR sequences set forth in Tables 3A-3D. The framework sequences for such anti-glyco-LAMP1 antibody and antigen-binding fragment can be the native murine framework sequences of the VH and VL sequences set forth in Tables 1A-1C or can be non-native (e.g., humanized or human) framework sequences.

[0012] In other aspects, an anti-glyco-LAMP1 antibody or antigen-binding fragment of the disclosure comprises heavy and/or light chain variable sequences of humanized anti-glyco-LAMP1 antibody 13C3 set forth in Tables 4A through 4G.

Table 1A 3C7.2C11.1C9 Sequences		
Description	Sequence	SEQ ID NO:
VH amino acid sequence (predicted mature)	EVKLEESGGGLVQPGGSMKVSCGASGFTFSDAWMDW VRQSPEKGLEWVAEMRSKAFNHAIYYAESVKGRFTISR DDSKSRVYLQMNLLRPEDTGIYYCTPNWDEGFAYWGQ GTLVTVSA	1
VL amino acid sequence (predicted mature)	DVMLTQTPLSLPVSLGDQASISCRSSQSLVHSNGNTYLH WYLQKPGQSPKLLINKVSNRFFGVPDRFSGSGSGTDFT LKISRVEAEDLGVYFCSQSTHVPRTFGGGTKLEIK	2
CDR-H1 amino acid sequence (IMGT definition)	GFTFSDAW	3
CDR-H2 amino acid sequence (IMGT definition)	MRSKAFNHAI	4
CDR-H3 amino acid sequence (IMGT definition)	TPNWDEGFAY	5
CDR-L1 amino acid sequence (IMGT definition)	QSLVHSNGNTY	6
CDR-L2 amino acid sequence (IMGT definition)	KVS	7
CDR-L3 amino acid sequence	SQSTHVPRT	8

Table 1A 3C7.2C11.1C9 Sequences		
Description	Sequence	SEQ ID NO:
(IMGT definition)		
CDR-H1 amino acid sequence (Kabat definition)	DAWMD	9
CDR-H2 amino acid sequence (Kabat definition)	EMRSKAFNHAIYYAESVKG	10
CDR-H3 amino acid sequence (Kabat definition)	NWDEGFAY	11
CDR-L1 amino acid sequence (Kabat definition)	RSSQSLVHSNGNTYLH	12
CDR-L2 amino acid sequence (Kabat definition)	KVSNRFF	13
CDR-L3 amino acid sequence (Kabat definition)	SQSTHVPRT	14
CDR-H1 amino acid sequence (Chothia definition)	GFTFSDA	15
CDR-H2 amino acid sequence (Chothia definition)	RSKAFNHA	16
CDR-H3 amino acid sequence (Chothia definition)	NWDEGFAY	17
CDR-L1 amino acid sequence (Chothia definition)	RSSQSLVHSNGNTYLH	18
CDR-L2 amino acid sequence (Chothia definition)	KVSNRFF	19
CDR-L3 amino acid sequence (Chothia definition)	SQSTHVPRT	20
VH nucleotide sequence (excl.	GAAGTGAAGCTTGAGGAGTCTGGAGGAGGCTTGCTG CAACCTGGAGGATCCATGAAAGTCTCTTGTGGTGCCT CTGGATTCACTTTTAGTGACGCCTGGATGGACTGGGT	21

Table 1A 3C7.2C11.1C9 Sequences		
Description	Sequence	SEQ ID NO:
signal sequence)	CCGCCAGTCTCCAGAGAAGGGGCTTGAGTGGGTTGC TGAGATGAGAAGCAAAGCTTTTAATCATGCAATATATT ATGCTGAGTCTGTGAAAGGGAGATTACCATTTCAAG AGATGATTCCAAAAGTAGAGTCTACCTGCAAATGAACT TGTTAAGACCTGAAGACACTGGCATTATTACTGTACC CCCAACTGGGACGAGGGGTTTGCTTACTGGGGCCAA GGGACTCTGGTCACTGTCTCTGCA	
VL nucleotide sequence (excl. signal sequence)	GATGTTATGCTGACCCAACTCCACTCTCCCTGCCTG TCAGTCTTGAGATCAAGCCTCCATCTCTTGACAGATCT AGTCAGAGCCTTGTACACAGTAATGGAAACACCTATTT ACATTGGTACCTGCAGAAGCCAGGCCAGTCTCCAAAG CTCCTGATCAACAAAGTTTCCAATCGATTTTTTGGGGT CCCAGACAGGTTTCAGTGGCAGTGGATCAGGGACAGA TTTCACACTCAAGATCAGCAGAGTGGAGGCTGAGGAT CTGGGAGTTTATTTCTGCTCTCAAAGCACACATGTTCC TCGGACGTTTCGGTGGAGGCACCAAGCTGGAAATCAA A	22

Table 1B 13C3.1C8.1C9 Sequences		
Description	Sequence	SEQ ID NO:
VH amino acid sequence (predicted mature)	EVKLEDSGGGLVQPGGSMKLSAASGFTFSDAWMDWV RHSPEKGLEWVAELRSKAFNHATYYAESVKGRFTISR DSKSTVYLQMNSLRAEDTGIYYCTPNWDEGFAYWGQG TLVTVSA	23
VL amino acid sequence (predicted mature)	DVVMQTPLSLPVSLGDQASISCRSSQSLVHSNGNTYLH WYLQKPGQSPKLLINKVSNRFSGVDPDRFSGSGSGTDF LKISRVEAEDLGVYFCSQSTHVPRTFGGGTKLEIK	24
CDR-H1 amino acid sequence (IMGT definition)	GFTFSDAW	25
CDR-H2 amino acid sequence (IMGT definition)	LRSKAFNHAT	26
CDR-H3 amino acid sequence (IMGT definition)	TPNWDEGFAY	27
CDR-L1 amino acid sequence (IMGT definition)	QSLVHSNGNTY	28
CDR-L2 amino acid sequence (IMGT definition)	KVS	29
CDR-L3 amino acid sequence	SQSTHVPRT	30

Table 1B 13C3.1C8.1C9 Sequences		
Description	Sequence	SEQ ID NO:
(IMGT definition)		
CDR-H1 amino acid sequence (Kabat definition)	DAWMD	31
CDR-H2 amino acid sequence (Kabat definition)	ELRSKAFNHATYYAESVKG	32
CDR-H3 amino acid sequence (Kabat definition)	NWDEGFAY	33
CDR-L1 amino acid sequence (Kabat definition)	RSSQSLVHSNGNTYLH	34
CDR-L2 amino acid sequence (Kabat definition)	KVSNRFS	35
CDR-L3 amino acid sequence (Kabat definition)	SQSTHVPRT	36
CDR-H1 amino acid sequence (Chothia definition)	GFTFSDA	37
CDR-H2 amino acid sequence (Chothia definition)	RSKAFNHA	38
CDR-H3 amino acid sequence (Chothia definition)	NWDEGFAY	39
CDR-L1 amino acid sequence (Chothia definition)	RSSQSLVHSNGNTYLH	40
CDR-L2 amino acid sequence (Chothia definition)	KVSNRFS	41
CDR-L3 amino acid sequence (Chothia definition)	SQSTHVPRT	42
VH nucleotide sequence (excl.	GAAGTGAAGCTTGAGGACTCTGGAGGAGGCTTGGTG CAACCTGGAGGATCCATGAACTCTCTTGTGCTGCCT CTGGATTCACTTTTAGTGACGCCTGGATGGACTGGGT	43

Table 1B 13C3.1C8.1C9 Sequences		
Description	Sequence	SEQ ID NO:
signal sequence)	CCGCCATTCTCCAGAGAAGGGGCTTGAGTGGGTTGC TGAACCTAGAAGCAAAGCTTTTAATCATGCAACATACT ATGCTGAGTCTGTGAAAGGGAGGTTCCACCATCTCAAG AGATGATTCCAAAAGTACAGTCTATCTGCAAAATGAACA GTTTAAGAGCTGAAGACACTGGCATTATTACTGTACT CCCAACTGGGACGAGGGGTTTGCTTACTGGGGCCAA GGGACTCTGGTCACTGTCTCTGCA	
VL nucleotide sequence (excl. signal sequence)	GATGTTGTGATGACCCAACTCCACTCTCCCTGCCTG TCAGTCTTGAGATCAGGCCTCCATCTCTTGAGATC TAGTCAGAGCCTTGACACAGTAATGGAAACACCTATT TAACTGGTACCTGCAGAAGCCAGGCCAGTCTCCAAA GCTCCTGATCAACAAAGTTTCCAACCGATTTTCTGGG GTCCCAGACAGGTTCAAGTGGCAGTGGATCAGGGACA GATTTCACTCAAGATCAGTAGAGTGGAGGCTGAGG ATCTGGGAGTTTATTTCTGCTCTCAAAGTACACATGTT CCTCGGACGTTCTGGTGGAGGCACCAAGCTGGAAATC AAA	44

Table 1C 13G2.1A10.2G5 Sequences		
Description	Sequence	SEQ ID NO:
VH amino acid sequence (predicted mature)	EVRLEESGGGLVQPGGSMKLSVASGFTFSDAWMDWV RQSPERGLEWVAELRSKTFNHATYYAESVRGRFTISR DSKSTVYLQMNSLRAEDTGIYYCSPNWDEGFAYWGQG TLVTVSA	45
VL amino acid sequence (predicted mature)	DVVMQIPLSLCVSLGDQASISCRSSQSLVHNNNGNTYLH WYLQKPGQSPKLLINKVSKRFTGVPDRFSGSGSGTDFT LKISRVEAEDLGVYFCSQSTHVPRTFGGGTKLEIK	46
CDR-H1 amino acid sequence (IMGT definition)	GFTFSDAW	47
CDR-H2 amino acid sequence (IMGT definition)	LRSKTFNHAT	48
CDR-H3 amino acid sequence (IMGT definition)	SPNWDEGFAY	49
CDR-L1 amino acid sequence (IMGT definition)	QSLVHNNNGNTY	50
CDR-L2 amino acid sequence (IMGT definition)	KVS	51
CDR-L3 amino acid sequence	SQSTHVPRT	52

Table 1C 13G2.1A10.2G5 Sequences		
Description	Sequence	SEQ ID NO:
(IMGT definition)		
CDR-H1 amino acid sequence (Kabat definition)	DAWMD	53
CDR-H2 amino acid sequence (Kabat definition)	ELRSKTFNHATYYAESVRG	54
CDR-H3 amino acid sequence (Kabat definition)	NWDEGFAY	55
CDR-L1 amino acid sequence (Kabat definition)	RSSQSLVHNNGNTYLH	56
CDR-L2 amino acid sequence (Kabat definition)	KVSKRFT	57
CDR-L3 amino acid sequence (Kabat definition)	SQSTHVPRT	58
CDR-H1 amino acid sequence (Chothia definition)	GFTFSDA	59
CDR-H2 amino acid sequence (Chothia definition)	RSKTFNHA	60
CDR-H3 amino acid sequence (Chothia definition)	NWDEGFAY	61
CDR-L1 amino acid sequence (Chothia definition)	RSSQSLVHNNGNTYLH	62
CDR-L2 amino acid sequence (Chothia definition)	KVSKRFT	63
CDR-L3 amino acid sequence (Chothia definition)	SQSTHVPRT	64
VH nucleotide sequence (excl.	GAAGTGAGGCTTGAGGAGTCTGGAGGAGGCTTGGTG CAACCTGGAGGATCCATGAACTCTCTTGTGTTGCCT CTGGATTCACTTTTAGTGACGCCTGGATGGACTGGGT	65

Table 1C 13G2.1A10.2G5 Sequences		
Description	Sequence	SEQ ID NO:
signal sequence)	CCGCCAGTCTCCAGAGAGGGGGCTTGAGTGGGTTGC TGAACCTTAGAAGCAAACTTTTAATCATGCGACATACT ATGCTGAGTCTGTGAGAGGGAGGTTACCATCTCAAG AGATGATTCCAAAAGTACTGTCTACCTGCAAATGAACA GTTTGAGAGCTGAAGACACTGGCATTATTTACTGTTCC CCCAACTGGGACGAGGGGTTTGCTTACTGGGGCCAA GGGACTCTGGTCACTGTCTCTGCA	
VL nucleotide sequence (excl. signal sequence)	GATGTTGTGATGACCCAAATCCACTCTCCCTGTGTGT CAGTCTTGGAGATCAAGCCTCCATCTCTTGCAGATCT AGTCAGAGCCTTGTACACAATAATGGAAACACCTATTT ACATTGGTACCTGCAGAAGCCAGGCCAGTCACCAAAG CTCCTGATCAACAAGGTTTCCAAGCGATTTACTGGGG TCCCAGACAGGTTCACTGGCAGTGGATCAGGGACAG ATTTCACTCAAGATCAGCAGAGTGGAGGCTGAGGA TCTGGGAGTTTATTTCTGCTCTCAAAGTACACATGTTCT CTCGGACGTTTCGGTGGAGGCACCAAGCTGGAAATCA AA	66

Table 1D CDR Consensus sequences – IMGT definition		
Description	Sequence	SEQ ID NO:
CDR-H1 amino acid sequence (IMGT definition)	GFTFSDAW	67
CDR-H2 amino acid sequence (IMGT definition)	X ₁ RSKX ₂ FNHAX ₃	68
CDR-H3 amino acid sequence (IMGT definition)	X ₅ PNWDEGFAY	69
CDR-L1 amino acid sequence (IMGT definition)	QSLVHX ₆ NGNTY	70
CDR-L2 amino acid sequence (IMGT definition)	KVS	71
CDR-L3 amino acid sequence (IMGT definition)	SQSTHVPRT	72
X ₁ = L or M; X ₂ = A or T; X ₃ = T or I; X ₅ = T or S; X ₆ = S or N		

Table 1E		
CDR Consensus sequences – Kabat definition		
Description	Sequence	SEQ ID NO:
CDR-H1 amino acid sequence (Kabat definition)	DAWMD	73
CDR-H2 amino acid sequence (Kabat definition)	EX ₁ RSKX ₂ FNHAX ₃ YYAESVX ₄ G	74
CDR-H3 amino acid sequence (Kabat definition)	NWDEGFAY	75
CDR-L1 amino acid sequence (Kabat definition)	RSSQSLVHX ₆ NGNTYLH	76
CDR-L2 amino acid sequence (Kabat definition)	KVSX ₇ RFX ₈	77
CDR-L3 amino acid sequence (Kabat definition)	SQSTHVPRT	78
X ₁ = L or M; X ₂ = A or T; X ₃ = T or I; X ₄ = K or R; X ₆ = S or N; X ₇ = N or K; X ₈ = S, F, or T		

Table 1F		
CDR Consensus sequences – Chothia definition		
Description	Sequence	SEQ ID NO:
CDR-H1 amino acid sequence (Chothia definition)	GFTFSDA	79
CDR-H2 amino acid sequence (Chothia definition)	RSKX ₂ FNHA	80
CDR-H3 amino acid sequence (Chothia definition)	NWDEGFAY	81
CDR-L1 amino acid sequence (Chothia definition)	RSSQSLVHX ₆ NGNTYLH	82
CDR-L2 amino acid sequence (Chothia definition)	KVSX ₇ RFX ₈	83
CDR-L3 amino acid sequence (Chothia definition)	SQSTHVPRT	84
X ₂ = A or T; X ₆ = S or N; X ₇ = N or K; X ₈ = S, F, or T		

Table 2A		
3C7.2C11.1C9 IMGT, Kabat, and Chothia CDR combined overlap sequences		
Description	Sequence	SEQ ID NO:
CDR-H1 amino acid sequence (combined overlap)	<u>GFTFSDA</u> WMD (IMGT) GFTFSD <u>AWMD</u> (Kabat) <u>GFTFSDA</u> WMD (Chothia)	85

Table 2A		
3C7.2C11.1C9 IMGT, Kabat, and Chothia CDR combined overlap sequences		
Description	Sequence	SEQ ID NO:
CDR-H2 amino acid sequence (combined overlap)	<u>EMRSKAFNHAI</u> YYAESVKG (IMGT) <u>EMRSKAFNHAI</u> YYAESVKG (Kabat) <u>EMRSKAFNHAI</u> YYAESVKG (Chothia)	86
CDR-H3 amino acid sequence (combined overlap)	<u>TPNWDEGFAY</u> (IMGT) TP <u>NWDEGFAY</u> (Kabat) TP <u>NWDEGFAY</u> (Chothia)	87
CDR-L1 amino acid sequence (combined overlap)	RSS <u>QSLVHSNGNTYLH</u> (IMGT) <u>RSSQSLVHSNGNTYLH</u> (Kabat) <u>RSSQSLVHSNGNTYLH</u> (Chothia)	88
CDR-L2 amino acid sequence (combined overlap)	<u>KVSNRFF</u> (IMGT) <u>KVSNRFF</u> (Kabat) <u>KVSNRFF</u> (Chothia)	89
CDR-L3 amino acid sequence (combined overlap)	<u>SQSTHVPRT</u> (IMGT) <u>SQSTHVPRT</u> (Kabat) <u>SQSTHVPRT</u> (Chothia)	90

Table 2B		
13C3.1C8.1C9 IMGT, Kabat, and Chothia CDR combined overlap sequences		
Description	Sequence	SEQ ID NO:
CDR-H1 amino acid sequence (combined overlap)	<u>GFTFSDAWMD</u> (IMGT) GFTFSD <u>AWMD</u> (Kabat) <u>GFTFSDAWMD</u> (Chothia)	91
CDR-H2 amino acid sequence (combined overlap)	<u>ELRSKAFNHAT</u> YYAESVKG (IMGT) <u>ELRSKAFNHAT</u> YYAESVKG (Kabat) <u>ELRSKAFNHAT</u> YYAESVKG (Chothia)	92
CDR-H3 amino acid sequence (combined overlap)	<u>TPNWDEGFAY</u> (IMGT) TP <u>NWDEGFAY</u> (Kabat) TP <u>NWDEGFAY</u> (Chothia)	93

Table 2B		
13C3.1C8.1C9 IMGT, Kabat, and Chothia CDR combined overlap sequences		
Description	Sequence	SEQ ID NO:
CDR-L1 amino acid sequence (combined overlap)	<u>RSSQSLVHSNGNTYLH</u> (IMGT)	94
	<u>RSSQSLVHSNGNTYLH</u> (Kabat)	
	<u>RSSQSLVHSNGNTYLH</u> (Chothia)	
CDR-L2 amino acid sequence (combined overlap)	<u>KVSNRFS</u> (IMGT)	95
	<u>KVSNRFS</u> (Kabat)	
	<u>KVSNRFS</u> (Chothia)	
CDR-L3 amino acid sequence (combined overlap)	<u>SQSTHVPRT</u> (IMGT)	96
	<u>SQSTHVPRT</u> (Kabat)	
	<u>SQSTHVPRT</u> (Chothia)	

Table 2C		
13G2.1A10.2G5 IMGT, Kabat, and Chothia CDR combined overlap sequences		
Description	Sequence	SEQ ID NO:
CDR-H1 amino acid sequence (combined overlap)	<u>GFTFSDAWMD</u> (IMGT)	97
	<u>GFTFSDAWMD</u> (Kabat)	
	<u>GFTFSDAWMD</u> (Chothia)	
CDR-H2 amino acid sequence (combined overlap)	<u>ELRSKTFNHATYYAESVRG</u> (IMGT)	98
	<u>ELRSKTFNHATYYAESVRG</u> (Kabat)	
	<u>ELRSKTFNHATYYAESVRG</u> (Chothia)	
CDR-H3 amino acid sequence (combined overlap)	<u>SPNWDEGFAY</u> (IMGT)	99
	<u>SPNWDEGFAY</u> (Kabat)	
	<u>SPNWDEGFAY</u> (Chothia)	
CDR-L1 amino acid sequence (combined overlap)	<u>RSSQSLVHNNGNTYLH</u> (IMGT)	100
	<u>RSSQSLVHNNGNTYLH</u> (Kabat)	
	<u>RSSQSLVHNNGNTYLH</u> (Chothia)	
CDR-L2 amino acid sequence (combined overlap)	<u>KVSKRFT</u> (IMGT)	101
	<u>KVSKRFT</u> (Kabat)	
	<u>KVSKRFT</u> (Chothia)	

Table 2C		
13G2.1A10.2G5 IMGT, Kabat, and Chothia CDR combined overlap sequences		
Description	Sequence	SEQ ID NO:
CDR-L3 amino acid sequence (combined overlap)	<u>SQSTHVPRT</u> (IMGT)	102
	<u>SQSTHVPRT</u> (Kabat)	
	<u>SQSTHVPRT</u> (Chothia)	

Table 2D		
CDR Consensus– IMGT, Kabat, and Chothia CDR combined overlap sequences		
Description	Sequence	SEQ ID NO:
CDR-H1 amino acid sequence (combined overlap)	GFTFSDAWMD	103
CDR-H2 amino acid sequence (combined overlap)	EX ₁ RSKX ₂ FNHAX ₃ YYAESVX ₄ G	104
CDR-H3 amino acid sequence (combined overlap)	X ₅ PNWDEGFAY	105
CDR-L1 amino acid sequence (combined overlap)	RSSQSLVHX ₆ NGNTYLH	106
CDR-L2 amino acid sequence (combined overlap)	KVSX ₇ RFX ₈	107
CDR-L3 amino acid sequence (combined overlap)	SQSTHVPRT	108
X ₁ = L or M; X ₂ = A or T; X ₃ = T or I; X ₄ = K or R; X ₅ = T or S; X ₆ = S or N; X ₇ = N or K; X ₈ = S, F, or T		

Table 3A		
3C7.2C11.1C9 IMGT, Kabat, and Chothia CDR common sequences		
Description	Sequence	SEQ ID NO:
CDR-H1 amino acid sequence (common sequence)	DA	109
CDR-H2 amino acid sequence (common sequence)	RSKAFNHA	110
CDR-H3 amino acid sequence (common sequence)	NWDEGFAY	111
CDR-L1 amino acid sequence (common sequence)	QSLVHSNGNTY	112
CDR-L2 amino acid sequence (common sequence)	KVS	113
CDR-L3 amino acid sequence (common sequence)	SQSTHVPRT	114

Table 3B		
13C3.1C8.1C9 IMGT, Kabat, and Chothia CDR common sequences		
Description	Sequence	SEQ ID NO:
CDR-H1 amino acid sequence (common sequence)	DA	115
CDR-H2 amino acid sequence (common sequence)	RSKAFNHA	116
CDR-H3 amino acid sequence (common sequence)	NWDEGFAY	117
CDR-L1 amino acid sequence (common sequence)	QSLVHSNGNTY	118
CDR-L2 amino acid sequence (common sequence)	KVS	119
CDR-L3 amino acid sequence (common sequence)	SQSTHVPRT	120

Table 3C		
13G2.1A10.2G5 IMGT, Kabat, and Chothia CDR common sequences		
Description	Sequence	SEQ ID NO:
CDR-H1 amino acid sequence (common sequence)	DA	121
CDR-H2 amino acid sequence (common sequence)	RSKTFNHA	122
CDR-H3 amino acid sequence (common sequence)	NWDEGFAY	123
CDR-L1 amino acid sequence (common sequence)	QSLVHNNGNTY	124
CDR-L2 amino acid sequence (common sequence)	KVS	125
CDR-L3 amino acid sequence (common sequence)	SQSTHVPRT	126

Table 3D		
Consensus CDR common sequences		
Description	Sequence	SEQ ID NO:
CDR-H1 amino acid sequence (common sequence)	DA	127
CDR-H2 amino acid sequence (common sequence)	SKX ₂ FNHA	128
CDR-H3 amino acid sequence (common sequence)	NWDEGFAY	129
CDR-L1 amino acid sequence (common sequence)	QSLVHX ₆ NGNTY	130
CDR-L2 amino acid sequence (common sequence)	KVS	131
CDR-L3 amino acid sequence (common sequence)	SQSTHVPRT	132
X ₂ = A or T; X ₆ = S or N		

Table 4A Humanized 13C3.1C8.1C9 Heavy Chain Sequences – Germline 3-23		
Description	Sequence	SEQ ID NO:
13C3-HV3-23-A	EVQLLES GGGGLVQP GGSRLS CAASGFTFSDAWMDW VRHAPGK GLEWVAELRSKAFNHATYYAESVKGRFTIS RDDSKNTVYLQMNSLRAEDTAVYYCTPNWDEGFAYW GGGTLTVSS	133
13C3-HV3-23-B	EVQLLES GGGGLVQP GGSRLS CAASGFTFSDAWMDW VRQAPGK GLEWVSELRSKAFNHATYYAESVKGRFTIS RDDSKNTLYLQMNSLRAEDTAVYYCTPNWDEGFAYW GGGTLTVSS	134
13C3-HV3-23-C	EVQLLES GGGGLVQP GGSRLS CAASGFTFSDAWMDW VRQAPGK GLEWVSEIRSSAFNHATYYAESVKGRFTISR DDSKNTLYLQMNSLRAEDTAVYYCTPNWDEGFAYWG GGGTLTVSS	135

Table 4B Humanized 13C3.1C8.1C9 Heavy Chain Sequences – Germline 3-15		
Description	Sequence	SEQ ID NO:
13C3-HV3-15-A	EVQLVES GGGGLVKP GGSRLS CAASGFTFSDAWMDW VRHAPGK GLEWVAELRSKAFNHATYYAESVKGRFTIS RDDSKNTVYLQMNSLKTEDTAVYYCTPNWDEGFAYW GGGTLTVSS	136
13C3-HV3-15-B	EVQLVES GGGGLVKP GGSRLS CAASGFTFSDAWMDW VRQAPGK GLEWVGELRSKAFNHATYYAESVKGRFTIS RDDSKNTLYLQMNSLKTEDTAVYYCTPNWDEGFAYW GGGTLTVSS	137
13C3-HV3-15-C	EVQLVES GGGGLVKP GGSRLS CAASGFTFSDAWMDW VRQAPGK GLEWVGEIRSKAFNHATYYAEPVKGRFTISR DDSKNTLYLQMNSLKTEDTAVYYCTPNWDEGFAYWG GGGTLTVSS	138

Table 4C Humanized 13C3.1C8.1C9 Heavy Chain Sequences – Germline 3-72		
Description	Sequence	SEQ ID NO:
13C3-HV3-72-A	EVQLVES GGGGLVQP GGSRLS CAASGFTFSDAWMDW VRHAPGK GLEWVAELRSKAFNHATYYAESVKGRFTIS RDDSKNSVYLQMNSLKTEDTAVYYCTPNWDEGFAYW GGGTLTVSS	139
13C3-HV3-72-B	EVQLVES GGGGLVQP GGSRLS CAASGFTFSDAWMDW VRQAPGK GLEWVGELRSKAFNHATYYAESVKGRFTIS RDDSKNSLYLQMNSLKTEDTAVYYCTPNWDEGFAYW GGGTLTVSS	140
13C3-HV3-72-C	EVQLVES GGGGLVQP GGSRLS CAASGFTFSDAWMDW VRQAPGK GLEWVGETRSKAFNYATYYAESVKGRFTIS RDDSKNSLYLQMNSLKTEDTAVYYCTPNWDEGFAYW GGGTLTVSS	141

Table 4D Humanized 13C3.1C8.1C9 Heavy Chain Sequences – Germline 7		
Description	Sequence	SEQ ID NO:
13C3-HV7-A	QVQLVQSGSELKKPGASVKVSKASGFTFSDAWMDW VRHAPGQGLEWVAELRSKAFNHATYYAESVKGRFVIS	142

Table 4D Humanized 13C3.1C8.1C9 Heavy Chain Sequences – Germline 7		
Description	Sequence	SEQ ID NO:
	RDDSVSTVYLQISSLKAEDTAVYYCTPNWDEGFAYWG QGTLTVSS	
13C3-HV7-B	QVQLVQSGSELKKPGASVKVSCASGYTFSDAWMDW VRQAPGQGLEWMGELRSKAFNHATYYAESVKGRFVIS RDDSVSTAYLQISSLKAEDTAVYYCAPNWDEGFAYWG QGTLTVSS	143
13C3-HV7-C	QVQLVQSGSELKKPGASVKVSCASGYTFTSAWMNW VRQAPGQGLEWMGEIRTNAFNHAPYYAQGVKGRFVIS RDDSVSTAYLQISSLKAEDTAVYYCAPNWDEGFAYWG QGTLTVSS	144

Table 4E Humanized 13C3.1C8.1C9 Light Chain Sequences – Germline 2		
Description	Sequence	SEQ ID NO:
13C3-KV2-A	DVVMTQSPSLPVTLGQPASISCRSSQSLVHSNGNTYL HWYQQRPQGQSPRLLINKVSNRFSQVDPDRFSGSGSGT DFTLKISRVEAEDVGVYFCSQSTHVPRTFGGGTKVEIK	145
13C3-KV2-B	DVVMTQSPSLPVTLGQPASISCRSSQSLVHSNGNTYL HWFQQRPQGQSPRLLINKVSNRFSQVDPDRFSGSGSGT DFTLKISRVEAEDVGVYYCSQSTHVPRTFGGGTKVEIK	146
13C3-KV2-C	DVVMTQSPSLPVTLGQPASISCRSSQSLVHSNANVYL HWFQQRPQGQSPRLLINKVSNRFSQVDPDRFSGSGSGT DFTLKISRVEAEDVGVYYCSQSTHVPRTFGGGTKVEIK	147

Table 4F Humanized 13C3.1C8.1C9 Light Chain Sequences – Germline 4		
Description	Sequence	SEQ ID NO:
13C3-KV4-A	DVVMTQSPDSLAVSLGERATINCRSSQSLVHSNGNTY LHWYQQKPGQPPKLLINKVSNRFSQVDPDRFSGSGSGT DFTLTISLQAEDVAVYFCSQSTHVPRTFGGGTKVEIK	148
13C3-KV4-B	DVVMTQSPDSLAVSLGERATINCKSSQSLHNSNGNTYL HWYQQKPGQPPKLLINKVSTRFSQVDPDRFSGSGSGTD FTLTISLQAEDVAVYYCSQSTHVPRTFGGGTKVEIK	149
13C3-KV4-C	DVVMTQSPDSLAVSLGERATINCKSSQSLHNSNANVYL HWYQQKPGQPPKLLINKASTRESQVDPDRFSGSGSGTD FTLTISLQAEDVAVYYCSQSTHVPRTFGGGTKVEIK	150

Table 4G Humanized 13C3.1C8.1C9 Light Chain Sequences – Germline 7		
Description	Sequence	SEQ ID NO:
13C3-KV7-A	DVVMTQSPASLAVSPGQRATITCRSSQSLVHSNGNTY LHWYQQKPGQPPKLLINKVSNRFSQVDPARFSGSGSGT DFTLTINPVEANDTANYFCSQSTHVPRTFGGGTKVEIK	151
13C3-KV7-B	DVWLTSQSPASLAVSPGQRATITCRSSESLSHSNGNTYL HWYQQKPGQPPKLLINKVSNKFTGVPARFSGSGSGTD FTLTINPVEANDTANYCYCSQSTHVPRTFGGGTKVEIK	152
13C3-KV7-C	DVWLTSQSPASLAVSPGQRATITCRASESLSHSNANVYI HWYQQKPGQPPKLLINKASNKFTGVPARFSGSGSGTD FTLTINPVEANDTANYCYCSQSTHVPRTFGGGTKVEIK	153

[0013] In certain aspects, an anti-glyco-LAMP1 antibody or antigen-binding fragment of the disclosure comprises CDRs comprising the amino acid sequences of any of the CDR combinations set forth in Tables 1A-3D. In certain embodiments, an anti-glyco-LAMP1 antibody or antigen-binding fragment of the disclosure comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:127, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:128, a CDR-H3 comprising the amino acid sequence of SEQ ID NO:129, a CDR-L1 comprising the amino acid sequence of SEQ ID NO:130, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:131, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:132. In some embodiments, CDR-H1 comprises the amino acid sequence of SEQ ID NO:127. In some embodiments, CDR-H2 comprises the amino acid sequence of SEQ ID NO:128. In some embodiments, CDR-H3 comprises the amino acid sequence of SEQ ID NO:129. In some embodiments, CDR-L1 comprises the amino acid sequence of SEQ ID NO:130. In some embodiments, CDR-L2 comprises the amino acid sequence of SEQ ID NO:131. In some embodiments, CDR-L3 comprises the amino acid sequence of SEQ ID NO:132.

[0014] In other aspects, an anti-glyco-LAMP1 antibody or antigen-binding fragment of the disclosure comprises heavy chain CDRs of SEQ ID NOS:3-5 and light chain CDRs of SEQ ID NOS:6-8. In other aspects, an anti-glyco-LAMP1 antibody or antigen-binding fragment of the disclosure comprises heavy chain CDRs of SEQ ID NOS:9-11 and light chain CDRs of SEQ ID NOS:12-14. In other aspects, an anti-glyco-LAMP1 antibody or antigen-binding fragment of the disclosure comprises heavy chain CDRs of SEQ ID NOS:15-17 and light chain CDRs of SEQ ID NOS:18-20. In other aspects, an anti-glyco-LAMP1 antibody or antigen-binding fragment of the disclosure comprises heavy chain CDRs of SEQ ID NOS:85-87 and light chain CDRs of SEQ ID NOS:88-90.

[0015] In other aspects, an anti-glyco-LAMP1 antibody or antigen-binding fragment of the disclosure comprises heavy chain CDRs of SEQ ID NOS:25-27 and light chain CDRs of SEQ ID NOS:28-30. In other aspects, an anti-glyco-LAMP1 antibody or antigen-binding fragment of the disclosure comprises heavy chain CDRs of SEQ ID NOS:31-33 and light chain CDRs of SEQ ID NOS:32-34. In other aspects, an anti-glyco-LAMP1 antibody or antigen-binding fragment of the disclosure comprises heavy chain CDRs of SEQ ID NOS:35-37 and light chain CDRs of SEQ ID NOS:38-40. In other aspects, an anti-glyco-LAMP1 antibody or antigen-binding fragment of the disclosure comprises heavy chain CDRs of SEQ ID NOS:91-93 and light chain CDRs of SEQ ID NOS:94-96.

[0016] In other aspects, an anti-glyco-LAMP1 antibody or antigen-binding fragment of the disclosure comprises heavy chain CDRs of SEQ ID NOS:47-49 and light chain CDRs of SEQ ID NOS:50-52. In other aspects, an anti-glyco-LAMP1 antibody or antigen-binding fragment of the disclosure comprises heavy chain CDRs of SEQ ID NOS:53-55 and light chain CDRs of SEQ ID NOS:56-58. In other aspects, an anti-glyco-LAMP1 antibody or antigen-binding

fragment of the disclosure comprises heavy chain CDRs of SEQ ID NOS:59-61 and light chain CDRs of SEQ ID NOS:62-64. In other aspects, an anti-glyco-LAMP1 antibody or antigen-binding fragment of the disclosure comprises heavy chain CDRs of SEQ ID NOS:97-99 and light chain CDRs of SEQ ID NOS:100-102.

[0017] In other aspects, an anti-glyco-LAMP1 antibody or antigen-binding fragment of the disclosure comprises heavy chain CDRs of SEQ ID NOS:67-69 and light chain CDRs of SEQ ID NOS:70-72. In other aspects, an anti-glyco-LAMP1 antibody or antigen-binding fragment of the disclosure comprises heavy chain CDRs of SEQ ID NOS:73-75 and light chain CDRs of SEQ ID NOS:76-78. In other aspects, an anti-glyco-LAMP1 antibody or antigen-binding fragment of the disclosure comprises heavy chain CDRs of SEQ ID NOS:79-81 and light chain CDRs of SEQ ID NOS:82-84. In other aspects, an anti-glyco-LAMP1 antibody or antigen-binding fragment of the disclosure comprises heavy chain CDRs of SEQ ID NOS:103-105 and light chain CDRs of SEQ ID NOS:106-108.

[0018] In certain embodiments, an anti-glyco-LAMP1 antibody or antigen-binding fragment of the disclosure comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:67, 73, 79, 85, 91, 97, 103, 109, 115, 121, or 127; a CDR-H2 comprising the amino acid sequence of SEQ ID NO:68, 74, 80, 86, 92, 98, 104, 110, 116, 122, or 128; a CDR-H3 comprising the amino acid sequence of SEQ ID NO:69, 75, 81, 87, 93, 99, 105, 111, 117, 123, or 129; a CDR-L1 comprising the amino acid sequence of SEQ ID NO:70, 76, 82, 88, 94, 100, 106, 112, 118, 124, or 130; a CDR-L2 comprising the amino acid sequence of SEQ ID NO:71, 77, 83, 89, 95, 101, 107, 113, 119, 125, or 131; and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:72, 78, 84, 90, 96, 102, 108, 114, 120, 126, or 132. EXPAND – SEE LAMP1 APPLICATION (paragraphs 14-17)

[0019] The antibodies and antigen-binding fragments of the disclosure can be murine, chimeric, humanized or human.

[0020] In further aspects, an anti-glyco-LAMP1 antibody or antigen binding fragment of the disclosure competes with an antibody or antigen binding fragment comprising heavy and light chain variable regions of SEQ ID NOS:1 and 2, respectively. In yet other aspects, the disclosure provides an anti-LAMP1 antibody or antigen binding fragment having heavy and light chain variable regions having at least 95%, 98%, 99%, or 99.5% sequence identity of SEQ ID NOS:1 and 2, respectively.

[0021] In yet other aspects, an anti-glyco-LAMP1 antibody or antigen binding fragment of the disclosure competes with an antibody or antigen binding fragment comprising heavy and light chain variable regions of SEQ ID NOS:23 and 24, respectively. In yet other aspects, the disclosure provides an anti-LAMP1 antibody or antigen binding fragment having heavy and light chain variable regions having at least 95%, 98%, 99%, or 99.5% sequence identity of SEQ ID NOS:23 and 24, respectively.

[0022] In yet other aspects, an anti-glyco-LAMP1 antibody or antigen binding fragment of the disclosure competes with an antibody or antigen binding fragment comprising heavy and light chain variable regions of SEQ ID NOS:45 and 46, respectively. In yet other aspects, the disclosure provides an anti-LAMP1 antibody or antigen binding fragment having heavy and light chain variable regions having at least 95%, 98%, 99%, or 99.5% sequence identity of SEQ ID NOS:45 and 46, respectively.

[0023] In yet other aspects, an anti-glyco-LAMP1 antibody or antigen binding fragment of the disclosure competes with an antibody or antigen binding fragment comprising a heavy chain variable region of any one of SEQ ID NOS:133-144 and a light chain variable region of any one of SEQ ID NOS:145-153. In yet other aspects, the disclosure provides an anti-LAMP1 antibody or antigen binding fragment having a heavy variable region having at least 95%, 98%, 99%, or 99.5% sequence identity of any one of SEQ ID NOS:133-134 and a light variable region having at least 95%, 98%, 99%, or 99.5% sequence identity of any one of SEQ ID NOS:145-153.

[0024] In yet other aspects, an anti-glyco-LAMP1 antibody or antigen-binding fragment of the disclosure is a single-chain variable fragment (scFv). An exemplary scFv comprises the heavy chain variable fragment N-terminal to the light chain variable fragment. In some embodiments, the scFv heavy chain variable fragment and light chain variable fragment are covalently bound to a linker sequence of 4-15 amino acids. The scFv can be in the form of a bi-specific T-cell engager or within a chimeric antigen receptor (CAR).

[0025] The anti-glyco-LAMP1 antibodies and antigen-binding fragments can be in the form of a multimer of a single-chain variable fragment, a bispecific single-chain variable fragment and a multimer of a bispecific single-chain variable fragment. In some embodiments, the multimer of a single chain variable fragment is selected a divalent single-chain variable fragment, a tribody or a tetrabody. In some of these embodiments, the multimer of a bispecific single-chain variable fragment is a bispecific T-cell engager.

[0026] Other aspects of the disclosure are drawn to nucleic acids encoding the anti-glyco-LAMP1 antibodies and antibody-binding fragments of the disclosure. In some embodiments, the portion of the nucleic acid nucleic acid encoding an anti-glyco-LAMP1 antibody or antigen-binding fragment is codon-optimized for expression in a human cell. In certain aspects, the disclosure provides an anti-glyco-LAMP1 antibody or antigen binding fragment having heavy and light chain variable regions encoded by a heavy chain nucleotide sequence having at least 95%, 98%, 99%, or 99.5% sequence identity to SEQ ID NO:21, 43, or 65 and a light chain nucleotide sequence having at least 95%, 98%, 99%, or 99.5% sequence identity to SEQ ID NO:22, 44 or 66. Vectors (e.g., a viral vector such as a lentiviral vector) and host cells comprising the nucleic acids are also within the scope of the disclosure. The heavy and light chains coding sequences can be present on a single vector or on separate vectors.

[0027] In yet another aspect of the disclosure is a pharmaceutical composition comprising an anti-glyco-LAMP1 antibody, antigen-binding fragment, nucleic acid (or pair of nucleic acids), vector (or pair of vectors) or host cell according to the disclosure, and a physiologically suitable buffer, adjuvant or diluent.

[0028] Still another aspect of the disclosure is a method of making a chimeric antigen receptor comprising incubating a cell comprising a nucleic acid or a vector according to the disclosure, under conditions suitable for expression of the coding region and collecting the chimeric antigen receptor.

[0029] Another aspect of the disclosure is a method of detecting cancer comprising contacting biological sample (e.g., a cell, tissue sample, or extracellular vesicle) with an anti-glyco-LAMP1 antibody or antigen-binding fragment of the disclosure and detecting whether the antibody is bound to the biological sample (e.g., cell, tissue sample, or extracellular vesicle).

[0030] Yet another aspect of the disclosure is an anti-glyco-LAMP1 antibody or antigen-binding fragment according to the disclosure of the disclosure for use in detecting cancer.

[0031] Yet another aspect of the disclosure is a method of treating cancer comprising administering a prophylactically or therapeutically effective amount of an anti-glyco-LAMP1 antibody, antigen-binding fragment, nucleic acid, vector, host cell or pharmaceutical composition according to the disclosure to a subject in need thereof.

[0032] Yet another aspect of the disclosure is an anti-glyco-LAMP1 antibody, antigen-binding fragment, nucleic acid, vector, host cell or pharmaceutical composition according to the disclosure for use in the treatment of cancer.

[0033] Yet another aspect of the disclosure is use of an anti-glyco-LAMP1 antibody, antigen-binding fragment, nucleic acid, vector, host cell or pharmaceutical composition according to the disclosure for the manufacture of a medicament for the treatment of cancer.

[0034] Glyco-LAMP1 peptides are also provided herein. The peptides can be 13-30 amino acids in length and comprise amino acids 1-11, 1-12, 1-13, 1-14, 1-15, 1-16, 1-17, 1-18, 1-19, 1-20, 2-11, 2-12, 2-13, 2-14, 2-15, 2-16, 2-17, 2-18, 2-19, 2-20, 3-11, 3-12, 3-13, 3-14, 3-15, 3-16, 3-17, 3-18, 3-19, 3-20, 4-11, 4-12, 4-13, 4-14, 4-15, 4-16, 4-17, 4-18, 4-19, 4-20, 5-11, 5-12, 5-13, 5-14, 5-15, 5-16, 5-17, 5-18, 5-19, 5-20, 6-11, 6-12, 6-13, 6-14, 6-15, 6-16, 6-17, 6-18, 6-19, or 6-20 of SEQ ID NO:200 (CEQDRPSP**T**TAPPAPPSPSP, glycosylated with GalNAc on the threonine residue shown in bold underlined text), SEQ ID NO:216 (CEQDRPSP**T**TAPPAPPSPSP (SEQ ID NO:216, glycosylated with GalNAc on the threonine residue shown in bold underlined text), SEQ ID NO:217 (CEQDRP**S****P**TAPPAPPSPSP, glycosylated with GalNAc on the threonine residue shown in bold underlined text), or SEQ ID NO:154 (CEQDRP**S****P****T**TAPPAPPSPSP, glycosylated with GalNAc on the serine and threonine residues shown in bold underlined text). The glyco-LAMP1 peptides are describe in Section

5.10 and numbered embodiments 739 to 765. The peptides can be included in a composition, as described in Section 5.10.1 and numbered embodiments 766 and 767. The glyco-LAMP1 peptides can be used in methods for producing antibodies in an animal and/or eliciting an immune response in an animal. Methods for using the glyco-LAMP1 peptides are described in Section 5.10.2 and numbered embodiments 768 to 771.

4. BRIEF DESCRIPTION OF THE FIGURES

[0035] FIGS. 1A-1B-5: Flow cytometry analysis of LAMP1 mouse antibodies on T47D COSMC-KO and T47D cells. FIG. 1A: Representative histograms for staining of 3C7.2C11.1C9, 13C3.1C8.1C9, and 13G2.1A10.2G5, anti-Golgi, mouse IgG isotype control, and anti-LAMP1 antibodies on T47D COSMC-KO and T47D cells. FIG. 1B1-1B4: Titration of 3C7.2C11.1C9, 13C3.1C8.1C9, and 13G2.1A10.2G5 on cell surface antigens found on T47D COSMC-KO and T47D cells. FIG. 1B-5: legend for FIG. 1B1 to 1B4.

[0036] FIG. 2: Immunofluorescence staining of 3C7.2C11.1C9, 13C3.1C8.1C9, 13G2.1A10.2G5, anti-LAMP1 and anti-Tn antibodies on T47D COSMC-KO and T47D cells.

[0037] FIG. 3: Immunohistochemistry of LAMP1 mouse antibodies, staining of 3C7.2C11.1C9, 13C3.1C8.1C9, and 13G2.1A10.2G5 antibodies on prostate cancer and normal tissues.

[0038] FIGS. 4A-1-4B-2: Immunohistochemistry of LAMP1 mouse antibodies. FIG. 4A-1: Staining of 13C3.1C8.1C9 antibody on FDA normal tissue microarray (FDA999x). Stats shown in FIGS. 4A-2 and 4A-3. FIG. 4B-1: Staining of 13C3.1C8.1C9 antibody on breast (TMA-BC08013d) and lung (TMA-LC121b) cancer tissues. Positive samples had ~70% of cancer cells that had strong cellular surface stain. Roughly 10-20% of analyzed cancer tissue had specific cellular surface stain ~70% of cancer cells. Stats shown in FIG. 4B-2.

[0039] FIGS. 5A-1-5B: Cell killing assay of LAMP1 ADCs. FIG. 5A-1-5A-3: Cytotoxicity of LAMP1 ADCs (3C7.2C11.1C9, 13C3.1C8.1C9, and 13G2.1A10.2G5, respectively) on T47D COSMC-KO cells. The drug conjugate was covalently linked DX8951 (with maleimide). FIG. 5B: Cytotoxicity of humanized LAMP1-ADC (13C3.1C8.1C9) on T47D COSMC-KO cells. The drug conjugate was covalently linked cleavable MMAE with maleimide (vc-PAB-MMAE). GO-13C3-Human-v1 is HV-72A/KV2A and GO-13C3-Human-v2 is HV23B/KV2A.

[0040] FIG. 6: Cell killing assay of LAMP1 CARTs, killing of LAMP1 CARTs (3C7.2C11.1C9, 13C3.1C8.1C9, and 13G2.1A10.2G5) on HaCAT COSMC-KO and HaCAT target cells with ratios of T cells to target cells (10:1).

[0041] FIG. 7: *In vivo* activity of mouse LAMP-ADC in solid tumor CDx mouse model. T47D COSMC-KO solid tumor model established by flank injection (CDx). The tumor volume at ADC injection was 100 mm³ and mice were treated with cleavable 13C3-vc-PAB-MMAE by IP injection (5 doses every 3 days with dose 1 at day 0). Tumor volume was measured by caliper.

[0042] FIGS. 8A-8C: Exemplary LAMP1 CART constructs 3C7-CART (FIG. 8A), 13C3-CART (FIG. 8B), and 13G2-CART (FIG. 8C). Testing of the constructs is described in Example 5.

[0043] FIGS. 9A-9B: Amino acid alignment of antibody heavy (FIG. 9A) and light (FIG. 9B) chains of wild type mAb237, 3C7.2C11.1C9 (3C7), 13C3.1C8.1C9 (13C3), and 13G2.1A10.2G5 (13G2). Depicted CDRs follow the IMGT definition.

5. DETAILED DESCRIPTION

5.1 Antibodies

[0044] The disclosure provides novel antibodies that are directed to a glycoform of LAMP1 present on tumor cells. These are exemplified by the antibodies 3C7.2C11.1C9 (hereinafter, “3C7”), 13C3.1C8.1C9 (hereinafter, “13C3”), and 13G2.1A10.2G5 (hereinafter, “13G2”). 3C7, 13C3, and 13G2 were identified in a screen for antibodies that bind to a glycosylated peptide present in LAMP1: CEQDRP**SP****TT**APPAPPSPSP (SEQ ID NO: 154), glycosylated with GalNAc on the serine and threonine residues shown in bold underlined text so as to mimic the glycosylation pattern of LAMP1 present on tumor cells.

[0045] The anti-glyco-LAMP1 antibodies of the disclosure, exemplified by antibodies 3C7, 13C3, and 13G2, are useful as tools in cancer diagnosis and therapy.

[0046] Thus, in certain aspects, the disclosure provides antibodies and antigen binding fragments that bind to a glycoform of LAMP1 present on tumor cells (referred to herein as “glyco-LAMP1”), and preferably to the peptide CEQDRP**SP****TT**APPAPPSPSP (SEQ ID NO:154), glycosylated with GalNAc on the serine and threonine residues shown in bold underlined text.

[0047] In other aspects, the disclosure provides antibodies and antigen binding fragments that bind to the peptide CEQDRPSP**TT**APPAPPSPSP (SEQ ID NO:200), glycosylated with GalNAc on the threonine residue shown in bold underlined text.

[0048] In other In other aspects, the disclosure provides antibodies and antigen binding fragments that bind to the peptide CEQDRPSP**TT**APPAPPSPSP (SEQ ID NO:216), glycosylated with GalNAc on the threonine residues shown in bold underlined text.

[0049] In other aspects, the disclosure provides antibodies and antigen binding fragments that bind to the peptide CEQDRP**SP****TT**APPAPPSPSP (SEQ ID NO:217), glycosylated with GalNAc on the serine and threonine residues shown in bold underlined text.

[0050] In certain aspects, the disclosure provides antibodies and antigen binding fragments that specifically compete for binding to a glyco-LAMP1 peptide described herein (e.g., one of SEQ ID NOS:154, 200, 216, and 217).

[0051] The anti-glyco-LAMP1 antibodies of the disclosure may be polyclonal, monoclonal, genetically engineered, and/or otherwise modified in nature, including but not limited to chimeric

antibodies, humanized antibodies, human antibodies, primatized antibodies, single chain antibodies, bispecific antibodies, dual-variable domain antibodies, *etc.* In various embodiments, the antibodies comprise all or a portion of a constant region of an antibody. In some embodiments, the constant region is an isotype selected from: IgA (*e.g.*, IgA₁ or IgA₂), IgD, IgE, IgG (*e.g.*, IgG₁, IgG₂, IgG₃ or IgG₄), and IgM. In specific embodiments, the anti-glyco-LAMP1 antibodies of the disclosure comprise an IgG₁ constant region isotype.

[0052] The term “monoclonal antibody” as used herein is not limited to antibodies produced through hybridoma technology. A monoclonal antibody is derived from a single clone, including any eukaryotic, prokaryotic, or phage clone, by any means available or known in the art. Monoclonal antibodies useful with the present disclosure can be prepared using a wide variety of techniques known in the art including the use of hybridoma, recombinant, and phage display technologies, or a combination thereof. In many uses of the present disclosure, including *in vivo* use of the anti-glyco-LAMP1 antibodies in humans, chimeric, primatized, humanized, or human antibodies can suitably be used.

[0053] The term “chimeric” antibody as used herein refers to an antibody having variable sequences derived from a non-human immunoglobulin, such as a rat or a mouse antibody, and human immunoglobulin constant regions, typically chosen from a human immunoglobulin template. Methods for producing chimeric antibodies are known in the art. See, *e.g.*, Morrison, 1985, *Science* 229(4719):1202-7; Oi *et al.*, 1986, *BioTechniques* 4:214-221; Gillies *et al.*, 1985, *J. Immunol. Methods* 125:191-202; U.S. Pat. Nos. 5,807,715; 4,816,567; and 4,816,397, which are incorporated herein by reference in their entireties.

[0054] “Humanized” forms of non-human (*e.g.*, murine) antibodies are chimeric immunoglobulins that contain minimal sequences derived from non-human immunoglobulin. In general, a humanized antibody will comprise substantially all of at least one, and typically two, variable domains, in which all or substantially all of the CDR regions correspond to those of a non-human immunoglobulin and all or substantially all of the framework regions (FR) are those of a human immunoglobulin sequence. The humanized antibody can also comprise at least a portion of an immunoglobulin constant region (Fc), typically that of a human immunoglobulin consensus sequence. Methods of antibody humanization are known in the art. See, *e.g.*, Riechmann *et al.*, 1988, *Nature* 332:323-7; U.S. Pat. Nos. 5,530,101; 5,585,089; 5,693,761; 5,693,762; and 6,180,370 to Queen *et al.*; EP239400; PCT publication WO 91/09967; U.S. Pat. No. 5,225,539; EP592106; EP519596; Padlan, 1991, *Mol. Immunol.*, 28:489-498; Studnicka *et al.*, 1994, *Prot. Eng.* 7:805-814; Roguska *et al.*, 1994, *Proc. Natl. Acad. Sci.* 91:969-973; and U.S. Pat. No. 5,565,332, all of which are hereby incorporated by reference in their entireties.

[0055] Exemplary humanized sequences are described in numbered embodiments 16 to 123. The variable region sequences for exemplary humanized antibodies and antigen-binding fragments thereof of the disclosure are set forth in Tables 4A-4G.

[0056] “Human antibodies” include antibodies having the amino acid sequence of a human immunoglobulin and include antibodies isolated from human immunoglobulin libraries or from animals transgenic for one or more human immunoglobulin and that do not express endogenous immunoglobulins. Human antibodies can be made by a variety of methods known in the art including phage display methods using antibody libraries derived from human immunoglobulin sequences. See U.S. Pat. Nos. 4,444,887 and 4,716,111; and PCT publications WO 98/46645; WO 98/50433; WO 98/24893; WO 98/16654; WO 96/34096; WO 96/33735; and WO 91/10741, each of which is incorporated herein by reference in its entirety. Human antibodies can also be produced using transgenic mice which are incapable of expressing functional endogenous immunoglobulins but which can express human immunoglobulin genes. See, *e.g.*, PCT publications WO 98/24893; WO 92/01047; WO 96/34096; WO 96/33735; U.S. Pat. Nos. 5,413,923; 5,625,126; 5,633,425; 5,569,825; 5,661,016; 5,545,806; 5,814,318; 5,885,793; 5,916,771; and 5,939,598, which are incorporated by reference herein in their entireties. Fully human antibodies that recognize a selected epitope can be generated using a technique referred to as “guided selection.” In this approach, a selected non-human monoclonal antibody, *e.g.*, a mouse antibody, is used to guide the selection of a completely human antibody recognizing the same epitope (see, Jespers *et al.*, 1988, *Biotechnology* 12:899-903).

[0057] “Primatized antibodies” comprise monkey variable regions and human constant regions. Methods for producing primatized antibodies are known in the art. See, *e.g.*, U.S. Pat. Nos. 5,658,570; 5,681,722; and 5,693,780, which are incorporated herein by reference in their entireties.

[0058] Anti-glyco-LAMP1 antibodies of the disclosure include both full-length (intact) antibody molecules, as well as antigen-binding fragments that are capable of binding glyco-LAMP1. Examples of antigen-binding fragments include by way of example and not limitation, Fab, Fab', F(ab')₂, Fv fragments, single chain Fv fragments and single domain fragments.

[0059] A Fab fragment contains the constant domain of the light chain (CL) and the first constant domain (CH1) of the heavy chain. Fab' fragments differ from Fab fragments by the addition of a few residues at the carboxyl terminus of the heavy chain CH1 domain including one or more cysteines from the antibody hinge region. F(ab') fragments are produced by cleavage of the disulfide bond at the hinge cysteines of the F(ab')₂ pepsin digestion product. Additional chemical couplings of antibody fragments are known to those of ordinary skill in the art. Fab and F(ab')₁ fragments lack the Fc fragment of intact antibody, clear more rapidly from the circulation of animals, and may have less non-specific tissue binding than an intact antibody (see, *e.g.*, Wahl *et al.*, 1983, *J. Nucl. Med.* 24:316).

[0060] An “Fv” fragment is the minimum fragment of an antibody that contains a complete target recognition and binding site. This region consists of a dimer of one heavy and one light

chain variable domain in a tight, non-covalent association (V_H - V_L dimer). It is in this configuration that the three CDRs of each variable domain interact to define a target binding site on the surface of the V_H - V_L dimer. Often, the six CDRs confer target binding specificity to the antibody. However, in some instances even a single variable domain (or half of an Fv comprising only three CDRs specific for a target) can have the ability to recognize and bind target, although at a lower affinity than the entire binding site.

[0061] “Single-chain Fv” or “scFv” antigen-binding fragments comprise the V_H and V_L domains of an antibody, where these domains are present in a single polypeptide chain. Generally, the Fv polypeptide further comprises a polypeptide linker between the V_H and V_L domains which enables the scFv to form the desired structure for target binding.

[0062] “Single domain antibodies” are composed of single V_H or V_L domains which exhibit sufficient affinity to glyco-LAMP1. In a specific embodiment, the single domain antibody is a camelized antibody (see, e.g., Riechmann, 1999, *Journal of Immunological Methods* 231:25-38).

[0063] The anti-glyco-LAMP1 antibodies of the disclosure may also be bispecific and other multiple specific antibodies. Bispecific antibodies are monoclonal, often human or humanized, antibodies that have binding specificities for two different epitopes on the same or different antigen. In the present disclosure, one of the binding specificities can be directed towards glyco-LAMP1, the other can be for any other antigen, e.g., for a cell-surface protein, receptor, receptor subunit, tissue-specific antigen, virally derived protein, virally encoded envelope protein, bacterially derived protein, or bacterial surface protein, *etc.* In certain embodiments, the bispecific and other multispecific anti-glyco-LAMP1 antibodies and antigen binding fragments specifically bind to a second LAMP1 epitope, an epitope on another protein co-expressed on cancer cells with LAMP1, or an epitope on another protein presented on a different cell, such as an activated T cell. Bispecific antibodies of the disclosure include IgG format bispecific antibodies and single chain-based bispecific antibodies.

[0064] IgG format bispecific antibodies of the disclosure can be any of the various types of IgG format bispecific antibodies known in the art, such as quadroma bispecific antibodies, “knobs-in-holes” bispecific antibodies, CrossMab bispecific antibodies (*i.e.*, bispecific domain-exchanged antibodies), charge paired bispecific antibodies, common light chain bispecific antibodies, one-arm single-chain Fab-immunoglobulin gamma bispecific antibodies, disulfide stabilized Fv bispecific antibodies, DuetMabs, controlled Fab-arm exchange bispecific antibodies, strand-exchange engineered domain body bispecific antibodies, two-arm leucine zipper heterodimeric monoclonal bispecific antibodies, $\kappa\lambda$ -body bispecific antibodies, dual variable domain bispecific antibodies, and cross-over dual variable domain bispecific antibodies. See, e.g., Köhler and Milstein, 1975, *Nature* 256:495-497; Milstein and Cuello, 1983, *Nature* 305:537-40; Ridgway *et al.*, 1996, *Protein Eng.* 9:617-621; Schaefer *et al.*, 2011,

Proc Natl Acad Sci USA 108:11187-92; Gunasekaran *et al.*, 2010, J Biol Chem 285:19637-46; Fischer *et al.*, 2015 Nature Commun 6:6113; Schanzer *et al.*, 2014, J Biol Chem 289:18693–706; Metz *et al.*, 2012 Protein Eng Des Sel 25:571–80; Mazor *et al.*, 2015 mAbs 7:377–89; Labrijn *et al.*, 2013 Proc Natl Acad Sci USA 110:5145–50; Davis *et al.*, 2010 Protein Eng Des Sel 23:195–202; Wranik *et al.*, 2012, J Biol Chem 287:43331–9; Gu *et al.*, 2015, PLoS One 10(5):e0124135; Steinmetz *et al.*, 2016, MAb 8(5):867-78; Klein *et al.*, 2016, MAb, 8(6):1010-1020; Liu *et al.*, 2017, Front. Immunol. 8:38; and Yang *et al.*, 2017, Int. J. Mol. Sci. 18:48, which are incorporated herein by reference in their entireties.

[0065] In some embodiments, the bispecific antibodies of the disclosure are domain exchanged antibodies referred to in the scientific and patent literature as CrossMabs. See, e.g., Schaefer *et al.*, 2011, Proc Natl Acad Sci USA 108:11187-92. The CrossMab technology is described in detail in WO 2009/080251, WO 2009/080252, WO 2009/080253, WO 2009/080254, WO 2013/026833, WO 2016/020309, and Schaefer *et al.*, 2011, Proc Natl Acad Sci USA 108:11187-92, which are incorporated herein by reference in their entireties. Briefly, the CrossMab technology is based on a domain crossover between heavy and light chains within one Fab-arm of a bispecific IgG, which promotes correct chain association. A CrossMab bispecific antibody of the disclosure can be a “CrossMab^{FAB}” antibody, in which the heavy and light chains of the Fab portion of one arm of a bispecific IgG antibody are exchanged. In other embodiments, a CrossMab bispecific antibody of the disclosure can be a “CrossMab^{VH-VL}” antibody, in which the only the variable domains of the heavy and light chains of the Fab portion of one arm of a bispecific IgG antibody are exchanged. In yet other embodiments, a CrossMab bispecific antibody of the disclosure can be a “CrossMab^{CH1-CL}” antibody, in which only the constant domains of the heavy and light chains of the Fab portion of one arm of a bispecific IgG antibody are exchanged. CrossMab^{CH1-CL} antibodies, in contrast to CrossMab^{FAB} and CrossMab^{VH-VL}, do not have predicted side products and, therefore, in some embodiments CrossMab^{CH1-CL} bispecific antibodies are preferred. See, Klein *et al.*, 2016, mAbs, 8(6):1010-1020.

[0066] In some embodiments, the bispecific antibodies of the disclosure are controlled Fab-arm exchange bispecific antibodies. Methods for making Fab-arm exchange bispecific antibodies are described in PCT Publication No. WO2011/131746 and Labrijn *et al.*, 2014 Nat Protoc. 9(10):2450-63, incorporated herein by reference in their entireties. Briefly, controlled Fab-arm exchange bispecific antibodies can be made by separately expressing two parental IgG1s containing single matching point mutations in the CH3 domain, mixing the parental IgG1s under redox conditions *in vitro* to enable recombination of half-molecules, and removing the reductant to allow reoxidation of interchain disulfide bonds, thereby forming the bispecific antibodies.

[0067] In some embodiments, the bispecific antibodies of the disclosure are “bottle opener,” “mAb-Fv,” “mAb-scFv,” “central-scFv,” “central-Fv,” “one-armed central-scFv” or “dual scFv”

format bispecific antibodies. Bispecific antibodies of these formats are described in PCT Publication No. WO 2016/182751, the contents of which are incorporated herein by reference in their entireties. Each of these formats relies on the self-assembling nature of Fc domains of antibody heavy chains, whereby two Fc subunit containing “monomers” assemble into a Fc domain containing “dimer.”

[0068] In the bottle opener format, the first monomer comprises a scFv covalently linked to the N-terminus of a Fc subunit, optionally via a linker, and the second monomer comprises a heavy chain (comprising a VH, CH1, and second Fc subunit). A bottle opener format bispecific antibody further comprises a light chain capable of pairing with the second monomer to form a Fab.

[0069] The mAb-Fv bispecific antibody format relies upon an “extra” VH domain attached to the C-terminus of one heavy chain monomer and an “extra” VL domain attached to the other heavy chain monomer, forming a third antigen binding domain. In some embodiments, a mAb-Fv bispecific antibody comprises a first monomer comprising a first VH domain, CH1 domain and a first Fc subunit, with a VL domain covalently attached to the C-terminus. The second monomer comprises a VH domain, a CH1 domain a second Fc subunit, and a VH covalently attached to the C-terminus of the second monomer. The two C-terminally attached variable domains make up a Fv. The mAb-Fv further comprises two light chains, which when associated with the first and second monomers form Fabs.

[0070] The mAb-scFv bispecific format relies on the use of a C-terminal attachment of a scFv to one of the monomers of a mAb, thus forming a third antigen binding domain. Thus, the first monomer comprises a first heavy chain (comprising a VH, CH1 and a first Fc subunit), with a C-terminally covalently attached scFv. mAb-scFv bispecific antibodies further comprise a second monomer (comprising a VH, CH1, and first Fc subunit) and two light chains, which when associated with the first and second monomers form Fabs.

[0071] The central-scFv bispecific format relies on the use of an inserted scFv domain in a mAb, thus forming a third antigen binding domain. The scFv domain is inserted between the Fc subunit and the CH1 domain of one of the monomers, thus providing a third antigen binding domain. Thus, the first monomer can comprise a VH domain, a CH1 domain (and optional hinge) and a first Fc subunit, with a scFv covalently attached between the C-terminus of the CH1 domain and the N-terminus of the first Fc subunit using optional domain linkers. The other monomer can be a standard Fab side monomer. Central-scFv bispecific antibodies further comprise two light chains, which when associated with the first and second monomers form Fabs.

[0072] The central-Fv bispecific format relies on the use of an inserted Fv domain thus forming a third antigen binding domain. Each monomer can contain a component of the Fv (e.g. one monomer comprises a variable heavy domain and the other a variable light domain). Thus, one

monomer can comprise a VH domain, a CH1 domain, a first Fc subunit and a VL domain covalently attached between the C-terminus of the CH1 domain and the N-terminus of the first Fc subunit, optionally using domain linkers. The other monomer can comprise a VH domain, a CH1 domain, a second Fc subunit and an additional VH domain covalently attached between the C-terminus of the CH1 domain and the N-terminus of the second Fc domain, optionally using domain linkers. Central-Fv bispecific antibodies further comprise two light chains, which when associated with the first and second monomers form Fabs.

[0073] The one-armed central-scFv bispecific format comprises one monomer comprising just a Fc subunit, while the other monomer comprises an inserted scFv domain thus forming a second antigen binding domain. Thus, one monomer can comprise a VH domain, a CH1 domain and a first Fc subunit, with a scFv covalently attached between the C-terminus of the CH1 domain and the N-terminus of the first Fc subunit, optionally using domain linkers. The second monomer can comprise an Fc domain. This embodiment further utilizes a light chain comprising a variable light domain and a constant light domain, that associates with the first monomer to form a Fab.

[0074] The dual scFv bispecific format comprises a first monomer comprising a scFv covalently attached to the N-terminus of a first Fc subunit, optionally via a linker, and second monomer comprising a scFv covalently attached to the N-terminus of a second Fc subunit, optionally via a linker.

[0075] Bispecific antibodies of the disclosure can comprise an Fc domain composed of a first and a second subunit. In one embodiment, the Fc domain is an IgG Fc domain. In a particular embodiment, the Fc domain is an IgG₁ Fc domain. In another embodiment the Fc domain is an IgG₄ Fc domain. In a more specific embodiment, the Fc domain is an IgG₄ Fc domain comprising an amino acid substitution at position S228 (Kabat EU index numbering), particularly the amino acid substitution S228P. Unless otherwise specified herein, numbering of amino acid residues in an Fc domain or constant region is according to the EU numbering system, also called the EU index, as described in Kabat *et al.*, 1991, Sequences of Proteins of Immunological Interest, 5th Ed. Public Health Service, National Institutes of Health, Bethesda, MD. This amino acid substitution reduces *in vivo* Fab arm exchange of IgG₄ antibodies (see Stubenrauch *et al.*, 2010, Drug Metabolism and Disposition 38:84-91). In a further particular embodiment, the Fc domain is a human Fc domain. In an even more particular embodiment, the Fc domain is a human IgG₁ Fc domain. An exemplary sequence of a human IgG₁ Fc region is:

DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVDVSHEDPEVKFNWYVDGVE
VHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREP
Q (SEQ ID NO: 156).

[0076] In particular embodiments, the Fc domain comprises a modification promoting the association of the first and the second subunit of the Fc domain. The site of most extensive protein-protein interaction between the two subunits of a human IgG Fc domain is in the CH3 domain. Thus, in one embodiment said modification is in the CH3 domain of the Fc domain.

[0077] In a specific embodiment said modification promoting the association of the first and the second subunit of the Fc domain is a so-called “knob-into-hole” modification, comprising a “knob” modification in one of the two subunits of the Fc domain and a “hole” modification in the other one of the two subunits of the Fc domain. The knob-into-hole technology is described e.g. in US 5,731,168; US 7,695,936; Ridgway *et al.*, 1996, Prot Eng 9:617-621, and Carter, J, 2001, Immunol Meth 248:7-15. Generally, the method involves introducing a protuberance (“knob”) at the interface of a first polypeptide and a corresponding cavity (“hole”) in the interface of a second polypeptide, such that the protuberance can be positioned in the cavity so as to promote heterodimer formation and hinder homodimer formation. Protuberances are constructed by replacing small amino acid side chains from the interface of the first polypeptide with larger side chains (e.g. tyrosine or tryptophan). Compensatory cavities of identical or similar size to the protuberances are created in the interface of the second polypeptide by replacing large amino acid side chains with smaller ones (e.g. alanine or threonine).

[0078] Accordingly, in some embodiments, an amino acid residue in the CH3 domain of the first subunit of the Fc domain is replaced with an amino acid residue having a larger side chain volume, thereby generating a protuberance within the CH3 domain of the first subunit which is positionable in a cavity within the CH3 domain of the second subunit, and an amino acid residue in the CH3 domain of the second subunit of the Fc domain is replaced with an amino acid residue having a smaller side chain volume, thereby generating a cavity within the CH3 domain of the second subunit within which the protuberance within the CH3 domain of the first subunit is positionable. Preferably said amino acid residue having a larger side chain volume is selected from the group consisting of arginine (R), phenylalanine (F), tyrosine (Y), and tryptophan (W). Preferably said amino acid residue having a smaller side chain volume is selected from the group consisting of alanine (A), serine (S), threonine (T), and valine (V). The protuberance and cavity can be made by altering the nucleic acid encoding the polypeptides, e.g. by site-specific mutagenesis, or by peptide synthesis.

[0079] In a specific such embodiment, in the first subunit of the Fc domain the threonine residue at position 366 is replaced with a tryptophan residue (T366W), and in the second subunit of the Fc domain the tyrosine residue at position 407 is replaced with a valine residue (Y407V) and optionally the threonine residue at position 366 is replaced with a serine residue (T366S) and the leucine residue at position 368 is replaced with an alanine residue (L368A) (numbering according to Kabat EU index). In a further embodiment, in the first subunit of the Fc domain additionally the serine residue at position 354 is replaced with a cysteine residue

(S354C) or the glutamic acid residue at position 356 is replaced with a cysteine residue (E356C) (particularly the serine residue at position 354 is replaced with a cysteine residue), and in the second subunit of the Fc domain additionally the tyrosine residue at position 349 is replaced by a cysteine residue (Y349C) (numbering according to Kabat EU index). In a particular embodiment, the first subunit of the Fc domain comprises the amino acid substitutions S354C and T366W, and the second subunit of the Fc domain comprises the amino acid substitutions Y349C, T366S, L368A and Y407V (numbering according to Kabat EU index).

[0080] In some embodiments, electrostatic steering (*e.g.*, as described in Gunasekaran *et al.*, 2010, J Biol Chem 285(25):19637-46) can be used to promote the association of the first and the second subunit of the Fc domain.

[0081] In some embodiments, the Fc domain comprises one or more amino acid substitutions that reduces binding to an Fc receptor and/or effector function.

[0082] In a particular embodiment the Fc receptor is an Fcγ receptor. In one embodiment the Fc receptor is a human Fc receptor. In one embodiment the Fc receptor is an activating Fc receptor. In a specific embodiment the Fc receptor is an activating human Fcγ receptor, more specifically human FcγRIIIa, FcγRI or FcγRIIa, most specifically human FcγRIIIa. In one embodiment the effector function is one or more selected from the group of complement dependent cytotoxicity (CDC), antibody-dependent cell-mediated cytotoxicity (ADCC), antibody-dependent cellular phagocytosis (ADCP), and cytokine secretion. In a particular embodiment, the effector function is ADCC.

[0083] Typically, the same one or more amino acid substitution is present in each of the two subunits of the Fc domain. In one embodiment, the one or more amino acid substitution reduces the binding affinity of the Fc domain to an Fc receptor. In one embodiment, the one or more amino acid substitution reduces the binding affinity of the Fc domain to an Fc receptor by at least 2-fold, at least 5-fold, or at least 10-fold.

[0084] In one embodiment, the Fc domain comprises an amino acid substitution at a position selected from the group of E233, L234, L235, N297, P331 and P329 (numberings according to Kabat EU index). In a more specific embodiment, the Fc domain comprises an amino acid substitution at a position selected from the group of L234, L235 and P329 (numberings according to Kabat EU index). In some embodiments, the Fc domain comprises the amino acid substitutions L234A and L235A (numberings according to Kabat EU index). In one such embodiment, the Fc domain is an IgG₁ Fc domain, particularly a human IgG₁ Fc domain. In one embodiment, the Fc domain comprises an amino acid substitution at position P329. In a more specific embodiment, the amino acid substitution is P329A or P329G, particularly P329G (numberings according to Kabat EU index). In one embodiment, the Fc domain comprises an amino acid substitution at position P329 and a further amino acid substitution at a position

selected from E233, L234, L235, N297 and P331 (numberings according to Kabat EU index). In a more specific embodiment, the further amino acid substitution is E233P, L234A, L235A, L235E, N297A, N297D or P331S. In particular embodiments, the Fc domain comprises amino acid substitutions at positions P329, L234 and L235 (numberings according to Kabat EU index). In more particular embodiments, the Fc domain comprises the amino acid mutations L234A, L235A and P329G (which can be referred to using the shorthand terms “P329G LALA”, “PGLALA” or “LALAPG”). Specifically, in particular embodiments, each subunit of the Fc domain comprises the amino acid substitutions L234A, L235A and P329G (Kabat EU index numbering), *i.e.* in each of the first and the second subunit of the Fc domain the leucine residue at position 234 is replaced with an alanine residue (L234A), the leucine residue at position 235 is replaced with an alanine residue (L235A) and the proline residue at position 329 is replaced by a glycine residue (P329G) (numbering according to Kabat EU index). In one such embodiment, the Fc domain is an IgG₁ Fc domain, particularly a human IgG₁ Fc domain.

[0085] Single chain-based bispecific antibodies of the disclosure can be any of the various types of single chain-based bispecific antibodies known in the art, such as bispecific T-cell engagers (BiTEs), diabodies, tandem diabodies (tandabs), dual-affinity retargeting molecules (DARTs), and bispecific killer cell engagers. See, *e.g.*, Löffler *et al.*, 2000, Blood 95:2098–103; Holliger *et al.*, 1993, Proc Natl Acad Sci USA, 90:6444–8; Kipriyanov *et al.*, 1999, Mol Biol 293:41–56; Johnson *et al.*, 2010, Mol Biol 399:436–49; Wiernik *et al.*, 2013, Clin Cancer Res 19:3844–55; Liu *et al.*, 2017, Front. Immunol. 8:38; and Yang *et al.*, 2017, Int. J. Mol. Sci. 18:48, which are incorporated herein by reference in their entireties.

[0086] In some embodiments, the bispecific antibodies of the disclosure are bispecific T-cell engagers (BiTEs). BiTEs are single polypeptide chain molecules having two antigen-binding domains, one of which binds to a T-cell antigen and the second of which binds to an antigen present on the surface of a target (see, PCT Publication WO 05/061547; Baeuerle *et al.*, 2008, Drugs of the Future 33: 137-147; Bargou, *et al.*, 2008, Science 321:974-977, incorporated herein by reference in their entireties). Thus, the BiTEs of the disclosure have an antigen binding domain that binds to a T-cell antigen, and a second antigen binding domain that is directed towards glyco-LAMP1.

[0087] In some embodiments, the bispecific antibodies of the disclosure are dual-affinity retargeting molecules (DARTs). DARTs comprise at least two polypeptide chains that associate (especially through a covalent interaction) to form at least two epitope binding sites, which may recognize the same or different epitopes. Each of the polypeptide chains of a DART comprise an immunoglobulin light chain variable region and an immunoglobulin heavy chain variable region, but these regions do not interact to form an epitope binding site. Rather, the immunoglobulin heavy chain variable region of one (*e.g.*, the first) of the DART polypeptide chains interacts with the immunoglobulin light chain variable region of a different (*e.g.*, the

second) DART™ polypeptide chain to form an epitope binding site. Similarly, the immunoglobulin light chain variable region of one (e.g., the first) of the DART polypeptide chains interacts with the immunoglobulin heavy chain variable region of a different (e.g., the second) DART polypeptide chain to form an epitope binding site. DARTs may be monospecific, bispecific, trispecific, etc., thus being able to simultaneously bind one, two, three or more different epitopes (which may be of the same or of different antigens). DARTs may additionally be monovalent, bivalent, trivalent, tetravalent, pentavalent, hexavalent, etc., thus being able to simultaneously bind one, two, three, four, five, six or more molecules. These two attributes of DARTs (*i.e.*, degree of specificity and valency may be combined, for example to produce bispecific antibodies (*i.e.*, capable of binding two epitopes) that are tetravalent (*i.e.*, capable of binding four sets of epitopes), *etc.* DART molecules are disclosed in PCT Publications WO 2006/113665, WO 2008/157379, and WO 2010/080538, which are incorporated herein by reference in their entireties.

[0088] In some embodiments of the bispecific antibodies of the disclosure, one of the binding specificities is directed towards glyco-LAMP1, and the other is directed to an antigen expressed on immune effector cells. The term “immune effector cell” or “effector cell” as used herein refers to a cell within the natural repertoire of cells in the mammalian immune system which can be activated to affect the viability of a target cell. Immune effector cells include cells of the lymphoid lineage such as natural killer (NK) cells, T cells including cytotoxic T cells, or B cells, but also cells of the myeloid lineage can be regarded as immune effector cells, such as monocytes or macrophages, dendritic cells and neutrophilic granulocytes. Hence, said effector cell is preferably an NK cell, a T cell, a B cell, a monocyte, a macrophage, a dendritic cell or a neutrophilic granulocyte. Recruitment of effector cells to aberrant cells means that immune effector cells are brought in close vicinity to the aberrant target cells such that the effector cells can directly kill, or indirectly initiate the killing of the aberrant cells that they are recruited to. In order to avoid non specific interactions it is preferred that the bispecific antibodies of the disclosure specifically recognize antigens on immune effector cells that are at least over-expressed by these immune effector cells compared to other cells in the body. Target antigens present on immune effector cells may include CD3, CD8, CD16, CD25, CD28, CD64, CD89, NKG2D and NKp46. Preferably, the antigen on immune effector cells is CD3 expressed on T cells.

[0089] As used herein, “CD3” refers to any native CD3 from any vertebrate source, including mammals such as primates (e.g. humans), non-human primates (e.g. cynomolgus monkeys) and rodents (e.g. mice and rats), unless otherwise indicated. The term encompasses “full-length,” unprocessed CD3 as well as any form of CD3 that results from processing in the cell. The term also encompasses naturally occurring variants of CD3, e.g., splice variants or allelic variants. The most preferred antigen on an immune effector cell is the CD3 epsilon chain. This

antigen has been shown to be very effective in recruiting T cells to aberrant cells. Hence, a bispecific antibody of the disclosure preferably specifically recognizes CD3 epsilon. The amino acid sequence of human CD3 epsilon is shown in UniProt (uniprot.org) accession no. P07766 (version 144), or NCBI (ncbi.nlm.nih.gov/) RefSeq NP_000724.1. The amino acid sequence of cynomolgus [*Macaca fascicularis*] CD3 epsilon is shown in NCBI GenBank no. BAB71849.1. For human therapeutic use, bispecific antibodies in which the CD3-binding domain specifically binds to human CD3 (e.g., the human CD3 epsilon chain) are used. For preclinical testing in non-human animals and cell lines, bispecific antibodies in which the CD3-binding domain specifically binds to the CD3 in the species utilized for the preclinical testing (e.g., cynomolgus CD3 for primate testing) can be used.

[0090] As used herein, a binding domain that “specifically binds to” or “specifically recognizes” a target antigen from a particular species does not preclude the binding to or recognition of the antigen from other species, and thus encompasses antibodies in which one or more of the binding domains have inter-species cross-reactivity. For example, a CD3-binding domain that “specifically binds to” or “specifically recognizes” human CD3 may also bind to or recognize cynomolgus CD3, and vice versa.

[0091] In some embodiments, a bispecific antibody of the disclosure can compete with monoclonal antibody H2C (described in PCT publication no. WO2008/119567) for binding an epitope of CD3. In other embodiments, a bispecific antibody of the disclosure can compete with monoclonal antibody V9 (described in Rodrigues *et al.*, 1992, Int J Cancer Suppl 7:45-50 and U.S. Pat. No. 6,054,297) for binding an epitope of CD3. In yet other embodiments, a bispecific antibody of the disclosure can compete with monoclonal antibody FN18 (described in Nooij *et al.*, 1986, Eur J Immunol 19:981-984) for binding an epitope of CD3. In yet other embodiments, a bispecific antibody of the disclosure can compete with monoclonal antibody SP34 (described in Pessano *et al.*, 1985, EMBO J 4:337-340) for binding an epitope of CD3.

[0092] In some embodiments, a bispecific antibody of the disclosure can compete with monoclonal antibody mAb1 (described in U.S. Pat. No. 10,730,944) for binding an epitope of CD8. In other embodiments, a bispecific antibody of the disclosure can compete with monoclonal antibody YTS169 (described in US2015/ 0191543) for binding an epitope of CD8. In other embodiments, a bispecific antibody of the disclosure can compete with monoclonal antibodies 4C9 5F4 (described in WO1987/005912) for binding an epitope of CD8.

[0093] In some embodiments, a bispecific antibody of the disclosure can compete with monoclonal antibody 3G8_ (described in WO2006/064136) for binding an epitope of CD16. In some embodiments, a bispecific antibody of the disclosure can compete with monoclonal antibody VEP13 (described in Ziegler-Heitbrock *et al.*, 1984, Clin.Exp. Immunol. 58:470-477) for binding an epitope of CD16. In some embodiments, a bispecific antibody of the disclosure

can compete with monoclonal antibody B73.1 (described in Perussia *et al.*, 1983, J. Immunol. 130(5):2142-2148) for binding an epitope of CD16.

[0094] In some embodiments, a bispecific antibody of the disclosure can compete with monoclonal antibody daclizumab and its variants (described in WO2014/145000) for binding an epitope of CD25. In some embodiments, a bispecific antibody of the disclosure can compete with monoclonal antibodies AB1, AB7, AB11, or AB12 (described in WO2004/045512) for binding an epitope of CD25. In some embodiments, a bispecific antibody of the disclosure can compete with monoclonal antibodies ALD25H1, ALD25H2, or ALD25H4 (described in WO2020/234399) for binding an epitope of CD25.

[0095] In some embodiments, a bispecific antibody of the disclosure can compete with monoclonal antibody FR104 (described in WO2017/103003) for binding an epitope of CD28. In some embodiments, a bispecific antibody of the disclosure can compete with monoclonal antibody hCD28.3 (described in WO2011/101791) for binding an epitope of CD28.

[0096] In some embodiments, a bispecific antibody of the disclosure can compete with monoclonal antibodies MS or 21 F2 (described in WO2009/077483) for binding an epitope of NKG2D. In some embodiments, a bispecific antibody of the disclosure can compete with monoclonal antibodies 5C5, 320, 230, 013, 296 or 395 (described in WO2021/009146) for binding an epitope of NKG2D. In some embodiments, a bispecific antibody of the disclosure can compete with monoclonal antibody KYK-2.0 (described in WO2010/017103) for binding an epitope of NKG2D.

[0097] The anti-glyco-LAMP1 antibodies of the disclosure include derivatized antibodies. For example, but not by way of limitation, derivatized antibodies are typically modified by glycosylation, acetylation, pegylation, phosphorylation, amidation, derivatization by known protecting/blocking groups, proteolytic cleavage, linkage to a cellular ligand or other protein. Any of numerous chemical modifications can be carried out by known techniques, including, but not limited to, specific chemical cleavage, acetylation, formylation, metabolic synthesis of tunicamycin, *etc.* Additionally, the derivative can contain one or more non-natural amino acids, *e.g.*, using ambrx technology (see, *e.g.*, Wolfson, 2006, Chem. Biol. 13(10):1011-2).

[0098] The anti-glyco-LAMP1 antibodies or binding fragments may be antibodies or fragments whose sequences have been modified to alter at least one constant region-mediated biological effector function. For example, in some embodiments, an anti-glyco-LAMP1 antibody may be modified to reduce at least one constant region-mediated biological effector function relative to the unmodified antibody, *e.g.*, reduced binding to the Fc receptor (FcγR). FcγR binding can be reduced by mutating the immunoglobulin constant region segment of the antibody at particular regions necessary for FcγR interactions (see, *e.g.*, Canfield and Morrison, 1991, J. Exp. Med. 173:1483-1491; and Lund *et al.*, 1991, J. Immunol. 147:2657-2662). Reduction in FcγR binding

ability of the antibody can also reduce other effector functions which rely on FcγR interactions, such as opsonization, phagocytosis and antigen-dependent cellular cytotoxicity ("ADCC").

[0099] The anti-glyco-LAMP1 antibody or binding fragments described herein include antibodies and/or binding fragments that have been modified to acquire or improve at least one constant region-mediated biological effector function relative to an unmodified antibody, *e.g.*, to enhance FcγR interactions (see, *e.g.*, US 2006/0134709). For example, an anti-glyco-LAMP1 antibody of the disclosure can have a constant region that binds FcγRIIA, FcγRIIB and/or FcγRIIIA with greater affinity than the corresponding wild type constant region.

[0100] Thus, antibodies of the disclosure may have alterations in biological activity that result in increased or decreased opsonization, phagocytosis, or ADCC. Such alterations are known in the art. For example, modifications in antibodies that reduce ADCC activity are described in U.S. Pat. No. 5,834,597. An exemplary ADCC lowering variant corresponds to "mutant 3" (shown in FIG. 4 of U.S. Pat. No. 5,834,597) in which residue 236 is deleted and residues 234, 235 and 237 (using EU numbering) are substituted with alanines. Another exemplary ADCC lowering variant comprises amino acid mutations L234A, L235A and P329G (which can be referred to using the shorthand term "P329G LALA"). The "P329G LALA" combination of amino acid substitutions almost completely abolishes Fcγ receptor (as well as complement) binding of a human IgG₁ Fc domain, as described in PCT publication no. WO 2012/130831, incorporated herein by reference in its entirety. WO 2012/130831 also describes methods of preparing such mutant Fc domains and methods for determining its properties such as Fc receptor binding or effector functions.

[0101] In some embodiments, the anti-glyco-LAMP1 antibodies of the disclosure have low levels of, or lack, fucose. Antibodies lacking fucose have been correlated with enhanced ADCC activity, especially at low doses of antibody. See Shields *et al.*, 2002, J. Biol. Chem. 277:26733-26740; Shinkawa *et al.*, 2003, J. Biol. Chem. 278:3466-73. Methods of preparing fucose-less antibodies include growth in rat myeloma YB2/0 cells (ATCC CRL 1662). YB2/0 cells express low levels of FUT8 mRNA, which encodes α-1, 6-fucosyltransferase, an enzyme necessary for fucosylation of polypeptides.

[0102] In some embodiments, the anti-glyco-LAMP1 antibodies or binding fragments include bisected oligosaccharides, *e.g.*, in which a biantennary oligosaccharide attached to an Fc domain is bisected by GlcNAc. Such variants may have reduced fucosylation and/or improved ADCC function as described above. Examples of such antibody variants are described, *e.g.*, in Umana *et al.*, 1999, Nat Biotechnol 17:176-180; Ferrara *et al.*, 2006, Biotechnol Bioeng 93: 851-861; WO 99/54342; WO 2004/065540; and WO 2003/011878.

[0103] In yet another aspect, the anti-glyco-LAMP1 antibodies or binding fragments include modifications that increase or decrease their binding affinities to the fetal Fc receptor, FcRn, for example, by mutating the immunoglobulin constant region segment at particular regions

involved in FcRn interactions (see, e.g., WO 2005/123780). In particular embodiments, an anti-glyco-LAMP1 antibody of the IgG class is mutated such that at least one of amino acid residues 250, 314, and 428 of the heavy chain constant region is substituted alone, or in any combinations thereof, such as at positions 250 and 428, or at positions 250 and 314, or at positions 314 and 428, or at positions 250, 314, and 428, with positions 250 and 428 a specific combination. For position 250, the substituting amino acid residue can be any amino acid residue other than threonine, including, but not limited to, alanine, cysteine, aspartic acid, glutamic acid, phenylalanine, glycine, histidine, isoleucine, lysine, leucine, methionine, asparagine, proline, glutamine, arginine, serine, valine, tryptophan, or tyrosine. For position 314, the substituting amino acid residue can be any amino acid residue other than leucine, including, but not limited to, alanine, cysteine, aspartic acid, glutamic acid, phenylalanine, glycine, histidine, isoleucine, lysine, methionine, asparagine, proline, glutamine, arginine, serine, threonine, valine, tryptophan, or tyrosine. For position 428, the substituting amino acid residues can be any amino acid residue other than methionine, including, but not limited to, alanine, cysteine, aspartic acid, glutamic acid, phenylalanine, glycine, histidine, isoleucine, lysine, leucine, asparagine, proline, glutamine, arginine, serine, threonine, valine, tryptophan, or tyrosine. Specific combinations of suitable amino acid substitutions are identified in Table 1 of U.S. Pat. No. 7,217,797, which is incorporated herein by reference. Such mutations increase binding to FcRn, which protects the antibody from degradation and increases its half-life.

[0104] In yet other aspects, an anti-glyco-LAMP1 antibody or antigen-binding fragment of the disclosure has one or more amino acids inserted into one or more of its hypervariable regions, for example as described in Jung and Pluckthun, 1997, *Protein Engineering* 10:9, 959-966; Yazaki *et al.*, 2004, *Protein Eng. Des Sel.* 17(5):481-9. Epub 2004 Aug. 17; and U.S. Pat. App. No. 2007/0280931.

[0105] In yet other aspects, particularly useful for diagnostic applications, an anti-glyco-LAMP1 antibody or antigen-binding fragment of the disclosure is attached to a detectable moiety. Detectable moieties include a radioactive moiety, a colorimetric molecule, a fluorescent moiety, a chemiluminescent moiety, an antigen, an enzyme, a detectable bead (such as a magnetic or electrodense (e.g., gold) bead), or a molecule that binds to another molecule (e.g., biotin or streptavidin)).

[0106] Radioisotopes or radionuclides may include ^3H , ^{14}C , ^{15}N , ^{35}S , ^{90}Y , ^{99}Tc , ^{111}In , ^{125}I , ^{131}I .

[0107] Fluorescent labels may include rhodamine, lanthanide phosphors, fluorescein and its derivatives, fluorochrome, GFP (GFP for "Green Fluorescent Protein"), dansyl, umbelliferone, phycoerythrin, phycocyanin, allophycocyanin, o-phthaldehyde, and fluorescamine.

[0108] Enzymatic labels may include horseradish peroxidase, β galactosidase, luciferase, alkaline phosphatase, glucose-6-phosphate dehydrogenase ("G6PDH"), alpha-D-galactosidase,

glucose oxidase, glucose amylase, carbonic anhydrase, acetylcholinesterase, lysozyme, malate dehydrogenase and peroxidase.

[0109] Chemiluminescent labels or chemiluminescers, such as isoluminol, luminol and the dioxetanes.

[0110] Other detectable moieties include molecules such as biotin, digoxigenin or 5-bromodeoxyuridine.

[0111] In yet other aspects, an anti-glyco-LAMP1 antibody or antigen-binding fragment of the disclosure may be used in a detection system to detect a biomarker in a sample, such as, *e.g.*, a patient-derived biological sample. The biomarker may be a protein biomarker (*e.g.*, a tumor-associated glycoform of LAMP-1, for example a glycoform of LAMP-1 comprising the amino acid sequence CEQDRPSP**T**TAPPAPPSPSP (SEQ ID NO:200) and glycosylated with GalNAc on the threonine residue shown in bold underlined text) present on the surface of or within, *e.g.*, a cancer cell (*e.g.*, from a tissue biopsy or a circulating tumor cell) or a cancer-derived extracellular vesicle).

[0112] Extracellular vesicles (EVs) are lipid membranous vesicles released from almost all cell types. EVs carry complex molecular cargoes, such as proteins, RNAs (*e.g.*, mRNA and noncoding RNAs (microRNA, transfer RNA, circular RNA and long noncoding RNA)), and DNA fragments. The molecular contents of EVs largely reflect the cell of origin and thus show cell-type specificity. In particular, cancer-derived EVs contain and present on their surfaces cancer-specific molecules expressed by parental cancer cells (see, *e.g.*, Yáñez-Mó *et al.*, 2015, J Extracell Vesicles. 4:27066; and Li *et al.*, 2015, Cell Res. 25:981-984)

[0113] In one embodiment, an anti-glyco-LAMP1 antibody or antigen-binding fragment of the disclosure is used in a method of detecting a biomarker in a sample comprising EVs (*e.g.*, a liquid biopsy). In such embodiments, the biomarker is recognized by the anti-glyco-LAMP1 antibody or antigen-binding fragment of the disclosure. The biomarker may be present on the surface of EVs. Exemplary methods of detecting the biomarker include, but are not limited to, immunoassays, such as immunoprecipitation; Western blot; ELISA; immunohistochemistry; immunocytochemistry; flow cytometry; and immuno-PCR. In some embodiments, an immunoassay can be a chemiluminescent immunoassay. In some embodiments, an immunoassay can be a high-throughput and/or automated immunoassay platform.¶

[0114] In some embodiments, the method of detecting a biomarker in a sample comprises contacting a sample with an anti-glyco-LAMP1 antibody or antigen-binding fragment of the disclosure. In some embodiments, such methods further comprise contacting the sample with one or more detection labels. In some embodiments, an anti-glyco-LAMP1 antibody or antigen-binding fragment of the disclosure is labeled with one or more detection labels.

[0115] In some embodiments, a capture assay is performed to selectively capture EVs from a sample such as a liquid biopsy sample exemplary examples of capture assays for EVs are described in US2021/0214806, which is hereby incorporated by reference in its entirety. In some embodiments, a capture assay is performed to selectively capture EVs of a certain size range, and/or certain characteristic(s), for example, EVs associated with cancer (e.g., a tumor-associated glycoform of LAMP-1, for example a glycoform of LAMP-1 comprising the amino acid sequence CEQDRPSP**T**TAPPAPPSPSP (SEQ ID NO:200) and glycosylated with GalNAc on the threonine residue shown in bold underlined text), glycosylated with GalNAc on the threonine residue shown in bold underlined text). In some such embodiments, prior to performing the capture assay, a sample may be pre-processed to remove non-EVs, including but not limited to, e.g., soluble proteins and interfering entities such as, e.g., cell debris. In some embodiments, EVs are purified from a sample using size exclusion chromatography.

[0116] In some embodiments, the method for detecting a biomarker comprises analyzing individual EVs (e.g., a single EV assay). For example, such an assay may involve (i) a capture assay such as an antibody capture assay and (ii) one or more detection assays for at least one or more additional biomarkers, wherein the capture assay is performed prior to the detection assay. See, e.g., US2021/0214806.

[0117] In some embodiments, a capture assay comprises a step of contacting a sample with at least one capture agent comprising an anti-glyco-LAMP1 antibody or antigen-binding fragment of the disclosure. The capture agent may be immobilized on a solid substrate. The solid substrate may be provided in a form that is suitable for capturing EVs and does not interfere with downstream handling, processing, and/or detection. For example, in some embodiments, a solid substrate may be or comprise a bead (e.g., a magnetic bead). In some embodiments, a solid substrate may be or comprise a surface. For example, in some embodiments, such a surface may be a capture surface of an assay chamber (e.g., a tube, a well, a microwell, a plate, a filter, a membrane, a matrix, etc.). In some embodiments, a capture agent is or comprises a magnetic bead comprising a capture moiety (e.g., an anti-glyco-LAMP1 antibody or antigen-binding fragment of the disclosure) conjugated thereto. See, e.g., US2021/0214806.

[0118] In certain aspects, an anti-glyco-LAMP1 antibody or antigen binding fragment of the disclosure competes with 3C7, or an antibody or antigen binding fragment comprising heavy and light chain variable regions of 3C7 (SEQ ID NOS:1 and 2, respectively).

[0119] In certain aspects, an anti-glyco-LAMP1 antibody or antigen binding fragment of the disclosure competes with 13C3 or an antibody or antigen binding fragment comprising heavy chain variable region of murine or humanized 13C3 (e.g., SEQ ID NO: 23 (murine) and SEQ ID NOS: 133-147 (exemplary humanized sequences)) and a light chain variable region of murine or humanized 13C3 (e.g., SEQ ID NO: 24 (murine) and SEQ ID NO: 148-153 (exemplary humanized sequences)).

[0120] In certain aspects, an anti-glyco-LAMP1 antibody or antigen binding fragment of the disclosure competes with 13G2, or an antibody or antigen binding fragment comprising heavy and light chain variable regions of 13G2 (SEQ ID NOS:45 and 46, respectively).

[0121] Competition can be assayed on cells that express the glyco-LAMP1 epitope bound by 3C7, 13C3, or 13G2 or on a glycosylated LAMP1 peptide containing the epitope bound by 3C7, 13C3, or 13G2, *e.g.*, (i) the peptide CEQDRPSP**IT**APPAPPSPSP (SEQ ID NO:200), glycosylated with GalNAc on the threonine residue shown in bold and underlined text; (ii) the peptide CEQDRPSP**IT**APPAPPSPSP (SEQ ID NO:216), glycosylated with GalNAc on the serine and threonine residues shown in bold and underlined text; (iii) the peptide CEQDRP**SP****IT**APPAPPSPSP (SEQ ID NO:217), glycosylated with GalNAc on the serine and threonine residues shown in bold and underlined text; and (iv) the peptide CEQDRP**SP****IT**APPAPPSPSP (SEQ ID NO:154), glycosylated with GalNAc on the serine and threonine residues shown in bold and underlined text. Cells that do not express the epitope or unglycosylated peptides (*e.g.*, CEQDRPSPTTAPPAPPSPSP; SEQ ID NO:155) can be used as controls.

[0122] Cells on which a competition assay can be carried out include but are not limited to the prostate, breast, skin cell lines (*e.g.*, breast cancer cell line T47D) and recombinant cells that are engineered to express the glyco-LAMP1 epitope. In one non-limiting example, T47D cells, which express LAMP1 but are inherently Tn-negative, are engineered to express the LAMP1 Tn-antigen by knockout of the COSMC chaperone. Wildtype cells expressing the unglycosylated form of LAMP1 can be used as a negative control.

[0123] Assays for competition include, but are not limited to, a radioactive material labeled immunoassay (RIA), an enzyme-linked immunosorbent assay (ELISA), a sandwich ELISA, fluorescence activated cell sorting (FACS) assays, surface plasmon resonance (*e.g.*, Biacore) assays, and bio-layer interferometry (BLI) assays. In some embodiments, antibody competition assays can be carried out using BLI (*e.g.*, using an Octet-HTX system (Molecular Devices)). Antibody competition or epitope binning of monoclonal antibodies can be assessed in tandem against their specific antigen using BLI. In a BLI assay, the antigen can be immobilized onto a biosensor and presented to two competing antibodies in consecutive steps. The binding to non-overlapping epitopes occurs if saturation with the first antibody does not block the binding of the second antibody. In some embodiments, antibody competition assays can be carried out using surface plasmon resonance (*e.g.*, using a Biacore system (Cytiva)). In a surface plasmon resonance assay, one or more antibodies can be immobilized onto a biosensor and presented with an analyte (*e.g.*, the glyco-LAMP1 peptides of SEQ ID NOS:154, 200, 216, or 217, or a negative control analyte such as an unglycosylated LAMP1 peptide of SEQ ID NO:155). In some embodiments, the antibodies are contacted with a saturating concentration of the analyte, for example a concentration of at least about 0.5 μ M. In some embodiments the saturating

concentration is about 1 μM , about 1.5 μM , or about 2 μM . When comparing the binding affinities of two antibodies, the affinities of both antibodies are preferably measured using the same concentration of both antibodies, e.g., measured using a 1 μM concentration of each antibody.

[0124] In conducting an antibody competition assay between a reference antibody and a test antibody (irrespective of species or isotype), one may first label the reference with a detectable label, such as a fluorophore, biotin or an enzymatic (or even radioactive) label to enable subsequent identification. In this case, cells expressing glyco-LAMP1 are incubated with unlabeled test antibody, labeled reference antibody is added, and the intensity of the bound label is measured. If the test antibody competes with the labeled reference antibody by binding to an overlapping epitope, the intensity will be decreased relative to a control reaction carried out without test antibody.

[0125] In a specific embodiment of this assay, the concentration of labeled reference antibody that yields 80% of maximal binding (" $\text{conc}_{80\%}$ ") under the assay conditions (e.g., a specified density of cells) is first determined, and a competition assay carried out with 10 x $\text{conc}_{80\%}$ of unlabeled test antibody and $\text{conc}_{80\%}$ of labeled reference antibody.

[0126] The inhibition can be expressed as an inhibition constant, or K_i , which is calculated according to the following formula:

$$K_i = \text{IC}_{50} / (1 + [\text{reference Ab concentration}] / K_d),$$

where IC_{50} is the concentration of test antibody that yields a 50% reduction in binding of the reference antibody and K_d is the dissociation constant of the reference antibody, a measure of its affinity for glyco-LAMP1. Antibodies that compete with anti-glyco-LAMP1 antibodies disclosed herein can have a K_i from 10 pM to 10 nM under assay conditions described herein.

[0127] In various embodiments, a test antibody is considered to compete with a reference antibody if it decreases binding of the reference antibody by at least about 20% or more, for example, by at least about 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 95% or even more, or by a percentage ranging between any of the foregoing values, at a reference antibody concentration that is 80% of maximal binding under the specific assay conditions used, and a test antibody concentration that is 10-fold higher than the reference antibody concentration.

[0128] In one example of a competition assay, the glycosylated LAMP1 peptide of one of SEQ ID NOS:154, 200, 216, or 217 is adhered onto a solid surface, e.g., a microwell plate, by contacting the plate with a solution of the peptide (e.g., at a concentration of 1 $\mu\text{g/mL}$ in PBS over night at 4°C). The plate is washed (e.g., 0.1% Tween 20 in PBS) and blocked (e.g., in Superblock, Thermo Scientific, Rockford, IL). A mixture of sub-saturating amount of biotinylated 3C7, 13C3, or 13G2 (e.g., at a concentration of 80 ng/mL) and unlabeled 3C7, 13C3, or 13G2 (the "reference" antibody) or competing anti-glyco-LAMP1 antibody (the "test" antibody)

antibody in serial dilution (e.g., at a concentration of 2.8 µg/mL, 8.3 µg/mL, or 25 µg/mL) in ELISA buffer (e.g., 1% BSA and 0.1% Tween 20 in PBS) is added to wells and plates are incubated for 1 hour with gentle shaking. The plate is washed, 1 µg/mL HRP-conjugated Streptavidin diluted in ELISA buffer is added to each well and the plates incubated for 1 hour. Plates are washed and bound antibodies were detected by addition of substrate (e.g., TMB, Biofx Laboratories Inc., Owings Mills, MD). The reaction is terminated by addition of stop buffer (e.g., Bio FX Stop Reagents, Biofx Laboratories Inc., Owings Mills, MD) and the absorbance is measured at 650 nm using microplate reader (e.g., VERSAmax, Molecular Devices, Sunnyvale, CA).

[0129] Variations on this competition assay can also be used to test competition between 3C7, 13C3, or 13G2 and another anti-glyco-LAMP1 antibody. For example, in certain aspects, the anti-glyco-LAMP1 antibody is used as a reference antibody and 3C7, 13C3, or 13G2 is used as a test antibody. Additionally, instead of a glycosylated LAMP1 peptide of one of SEQ ID NOS:154, 200, 216, or 217, a membrane-bound glyco-LAMP1 expressed on the cell surface (for example on the surface of one of the cell types mentioned above) in culture can be used. Generally, about 10^4 to 10^6 transfectants, e.g., about 10^5 transfectants, are used. Other formats for competition assays are known in the art and can be employed.

[0130] In various embodiments, an anti-glyco-LAMP1 antibody of the disclosure reduces the binding of labeled 3C7, 13C3, or 13G2 by at least 40%, by at least 50%, by at least 60%, by at least 70%, by at least 80%, by at least 90%, or by a percentage ranging between any of the foregoing values (e.g., an anti-glyco-LAMP1 antibody of the disclosure reduces the binding of labeled 3C7, 13C3, or 13G2 by 50% to 70%) when the anti-glyco-LAMP1 antibody is used at a concentration of 0.08 µg/mL, 0.4 µg/mL, 2 µg/mL, 10 µg/mL, 50 µg/mL, 100 µg/mL or at a concentration ranging between any of the foregoing values (e.g., at a concentration ranging from 2 µg/mL to 10 µg/mL).

[0131] In other embodiments, 3C7, 13C3, or 13G2 reduces the binding of a labeled anti-glyco-LAMP1 antibody of the disclosure by at least 40%, by at least 50%, by at least 60%, by at least 70%, by at least 80%, by at least 90%, or by a percentage ranging between any of the foregoing values (e.g., 3C7, 13C3, or 13G2 reduces the binding of a labeled an anti-glyco-LAMP1 antibody of the disclosure by 50% to 70%) when 3C7, 13C3, or 13G2 is used at a concentration of 0.4 µg/mL, 2 µg/mL, 10 µg/mL, 50 µg/mL, 250 µg/mL or at a concentration ranging between any of the foregoing values (e.g., at a concentration ranging from 2 µg/mL to 10 µg/mL).

[0132] In the foregoing assays, the 3C7, 13C3, or 13G2 antibody can be replaced by any antibody or antigen-binding fragment comprising the CDRs or the heavy and light chain variable regions of 3C7, 13C3, or 13G2, such as a humanized or chimeric counterpart of 3C7, 13C3, or

13G2. Exemplary humanized heavy and light chain variable regions of 13C3 are provided in Tables 4A-4G.

[0133] In certain aspects, an anti-glyco-LAMP1 antibody or antigen-binding fragment of the disclosure has an epitope which is the same or similar to the epitope of 3C7, 13C3, or 13G2. The epitope of an anti-glyco-LAMP1 antibody or antigen-binding fragment of the disclosure can be characterized by performing, for example, alanine scanning. A library of glycopeptides, each varying from the LAMP1 glycopeptide (SEQ ID NO:154) by an alanine point mutation at one amino acid position of SEQ ID NO:154 (or, where the LAMP1 peptide has an alanine, by a glycine point mutation). By measuring an antibody or antigen binding fragment's binding to each of the peptides by ELISA, the antibody or antigen binding fragment's epitope can be mapped.

[0134] In certain aspects, an anti-glyco-LAMP1 antibody or antigen-binding fragment of the disclosure comprises heavy and/or light chain variable sequences (or encoded by the nucleotide sequences) set forth in Tables 1A-1C (murine) and 4A-4G (humanized). In other aspects, an anti-glyco-LAMP1 antibody or antigen-binding fragment of the disclosure comprises heavy and/or light chain CDR sequences (or encoded by the nucleotide sequences) set forth in Tables 1A-3D. The framework sequences for such anti-glyco-LAMP1 antibody and antigen-binding fragment can be the native murine framework sequences of the VH and VL sequences set forth in Tables 1A-1C or can be non-native (e.g., humanized or human) framework sequences. Humanized framework sequences of the VH and VL sequences of 13C3 are set forth in Tables 4A-4G.

[0135] In yet other aspects, the disclosure provides an anti-LAMP1 antibody or antigen binding fragment having heavy and light chain variable regions having at least 95%, 98%, 99%, or 99.5% sequence identity of SEQ ID NOS: 1 and 2, respectively.

[0136] In yet other aspects, the disclosure provides an anti-LAMP1 antibody or antigen binding fragment having heavy and light chain variable regions having at least 95%, 98%, 99%, or 99.5% sequence identity of SEQ ID NOS: 23 and 24, respectively.

[0137] In yet other aspects, the disclosure provides an anti-LAMP1 antibody or antigen binding fragment having heavy and light chain variable regions having at least 95%, 98%, 99%, or 99.5% sequence identity of SEQ ID NOS: 45 and 46, respectively.

[0138] In yet other aspects, the disclosure provides an anti-LAMP1 antibody or antigen binding fragment having a heavy chain variable region having at least 95%, 98%, 99%, or 99.5% sequence identity of one of SEQ ID NOS:133-147 and light chain variable regions having at least 95%, 98%, 99%, or 99.5% sequence identity of one of SEQ ID NOS:148-153.

[0139] In yet other aspects, an anti-glyco-LAMP1 antibody or antigen-binding fragment of the disclosure is a single-chain variable fragment (scFv). An exemplary scFv comprises the heavy

chain variable fragment N-terminal to the light chain variable fragment. Another exemplary scFv comprises the light chain variable fragment N-terminal to the heavy chain variable fragment. In some embodiments, the scFv heavy chain variable fragment and light chain variable fragment are covalently bound to a linker sequence of 4-15 amino acids. The scFv can be in the form of a bi-specific T-cell engager or within a chimeric antigen receptor (CAR).

5.1.1. Antibody Specificity

[0140] In some embodiments, the anti-glyco-LAMP1 antibodies of the disclosure specifically bind to the LAMP1 glycoprotein CEQDRPSP**T**TAPPAPPSPSP (SEQ ID NO:200), glycosylated with GalNAc on the threonine residue shown in bold underlined text.

[0141] In other embodiments, the anti-glyco-LAMP1 antibodies of the disclosure specifically bind to the LAMP1 glycoprotein CEQDRPSP**TT**TAPPAPPSPSP (SEQ ID NO:216), glycosylated with GalNAc on the threonine residues shown in bold underlined text.

[0142] In yet other embodiments, the anti-glyco-LAMP1 antibodies of the disclosure specifically bind to the LAMP1 glycoprotein CEQDRP**SPT**TAPPAPPSPSP (SEQ ID NO:217), glycosylated with GalNAc on the serine and threonine residues shown in bold underlined text.

[0143] In some embodiments, the anti-glyco-LAMP1 antibodies of the disclosure specifically bind to the LAMP1 glycoprotein CEQDRP**SPTT**TAPPAPPSPSP (SEQ ID NO:154), glycosylated with GalNAc on the serine and threonine residues shown in bold underlined text.

[0144] In certain embodiments, the anti-glyco-LAMP1 antibodies of the disclosure specifically binds to a LAMP1 glycoprotein described above, and does not specifically bind to one or more of: the unglycosylated LAMP1 peptide CEQDRP**SPTT**TAPPAPPSPSP (SEQ ID NO: 155) (the “unglycosylated LAMP1 peptide”); the MUC1 tandem repeat (VTSAPDTRPAPGSTAPPAHG)₃ (SEQ ID NO:208) that has been glycosylated *in vitro* using purified recombinant human glycosyltransferases GalNAc-T1, GalNAc-T2, and GalNAc-T4 (“the first MUC1 glycopeptide”); the MUC1 peptide TAPPAHGVT**TS**APD**TR**PAPG**ST**APPAHGVT (SEQ ID NO:209) that has been glycosylated *in vitro* with GalNAc on the serine and threonine residues shown with bold and underlined text (the “second MUC1 glycopeptide”); the podoplanin peptide ERG**TK**PPLLEELSGK (SEQ ID NO:211) that has been glycosylated *in vitro* with GalNAc on the threonine residue shown with bold and underlined text (the “PDPN glycopeptide”); the CD44v6 peptide GYRQ**TP**KEDSH**ST**TGTAAA (SEQ ID NO:212) that has been glycosylated *in vitro* with GalNAc on the threonine and serine residues shown with bold and underlined text (the “CD44v6 glycopeptide”); the MUC4 peptide CTIPSTAMHTR**STA**APIILP (SEQ ID NO:213) that has been glycosylated *in vitro* with GalNAc on the serine and threonine residues shown with bold and underlined text (the “MUC4 glycopeptide”); and the cMET peptide PTKSFISGG**ST**ITGVGKNLN (SEQ ID NO:214) that has been glycosylated *in vitro* with GalNAc

on the serine and threonine residues shown with bold and underlined text (the “cMET glycopeptide”).

[0145] In some embodiments, an anti-glyco-LAMP1 antibody of the disclosure has a binding affinity to the LAMP1 glycopeptide which is at least 3 times, at least 5 times, at least 10 times, at least 20 times, at least 50 times, at least 100 times, or at least 1000 times the binding affinity of the anti-glyco-LAMP1 antibody to the unglycosylated LAMP1 peptide.

[0146] In some embodiments, an anti-glyco-LAMP1 antibody of the disclosure has a binding affinity to the LAMP1 glycopeptide which is at least 3 times, at least 5 times, at least 10 times, at least 20 times, at least 50 times, at least 100 times, or at least 1000 times the binding affinity of the anti-glyco-LAMP1 antibody to the first MUC1 glycopeptide.

[0147] In some embodiments, an anti-glyco-LAMP1 antibody of the disclosure has a binding affinity to the LAMP1 glycopeptide which is at least 3 times, at least 5 times, at least 10 times, at least 20 times, at least 50 times, at least 100 times, or at least 1000 times the binding affinity of the anti-glyco-LAMP1 antibody to the second MUC1 glycopeptide.

[0148] In some embodiments, an anti-glyco-LAMP1 antibody of the disclosure has a binding affinity to the LAMP1 glycopeptide which is at least 3 times, at least 5 times, at least 10 times, at least 20 times, at least 50 times, at least 100 times, or at least 1000 times the binding affinity of the anti-glyco-LAMP1 antibody to the PDPN glycopeptide.

[0149] In some embodiments, an anti-glyco-LAMP1 antibody of the disclosure has a binding affinity to the LAMP1 glycopeptide which is at least 3 times, at least 5 times, at least 10 times, at least 20 times, at least 50 times, at least 100 times, or at least 1000 times the binding affinity of the anti-glyco-LAMP1 antibody to the CD44v6 glycopeptide.

[0150] In some embodiments, an anti-glyco-LAMP1 antibody of the disclosure has a binding affinity to the LAMP1 glycopeptide which is at least 3 times, at least 5 times, at least 10 times, at least 20 times, at least 50 times, at least 100 times, or at least 1000 times the binding affinity of the anti-glyco-LAMP1 antibody to the MUC4 glycopeptide.

[0151] In some embodiments, an anti-glyco-LAMP1 antibody of the disclosure has a binding affinity to the LAMP1 glycopeptide which is at least 3 times, at least 5 times, at least 10 times, at least 20 times, at least 50 times, at least 100 times, or at least 1000 times the binding affinity of the anti-glyco-LAMP1 antibody to the cMET glycopeptide.

[0152] Assays for determining affinity, including relative affinity, include but are not limited to a radioactive material labeled immunoassay (RIA), an enzyme-linked immunosorbent assay (ELISA), a sandwich ELISA, fluorescence activated cell sorting (FACS) assays, surface plasmon resonance (e.g., Biacore) assays, and bio-layer interferometry (BLI) assays. In some embodiments, affinity is measured by surface plasmon resonance (e.g., Biacore). In other embodiments, affinity

[0153] Exemplary anti-glyco-LAMP1 antibody and fragments thereof are described in numbered embodiments 1 to 526.

5.2 Antibody-Drug Conjugates

[0154] Another aspect of the disclosure concerns antibody drug conjugates (ADCs) including the anti-glyco-LAMP1 antibodies and antigen-binding fragments of the disclosure. The ADCs generally comprise an anti-glyco-LAMP1 antibody and/or binding fragment as described herein having one or more cytotoxic and/or cytostatic agents linked thereto by way of one or more linkers. In specific embodiments, the ADCs are compounds according to structural formula (I):



or salts thereof, where each "D" represents, independently of the others, a cytotoxic and/or cytostatic agent ("drug"); each "L" represents, independently of the others, a linker; "Ab" represents an anti-glyco-LAMP1 antigen binding domain, such as an anti-glyco-LAMP1 antibody or binding fragment described herein; each "XY" represents a linkage formed between a functional group R^x on the linker and a "complementary" functional group R^y on the antibody, and n represents the number of drugs linked to, or drug-to-antibody ratio (DAR), of the ADC.

[0155] Specific embodiments of the various antibodies (Ab) that can comprise the ADCs include the various embodiments of anti-glyco-LAMP1 antibodies and/or binding fragments described above.

[0156] In some specific embodiments of the ADCs and/or salts of structural formula (I), each D is the same and/or each L is the same.

[0157] Specific embodiments of cytotoxic and/or cytostatic agents (D) and linkers (L) that can comprise the anti-glyco-LAMP1 ADCs of the disclosure, as well as the number of cytotoxic and/or cytostatic agents linked to the ADCs, are described in more detail below.

5.2.1. Cytotoxic and/or Cytostatic Agents

[0158] The cytotoxic and/or cytostatic agents may be any agents known to inhibit the growth and/or replication of and/or kill cells, and in particular cancer and/or tumor cells. Numerous agents having cytotoxic and/or cytostatic properties are known in the literature. Non-limiting examples of classes of cytotoxic and/or cytostatic agents include, by way of example and not limitation, radionuclides, alkylating agents, topoisomerase I inhibitors, topoisomerase II inhibitors, DNA intercalating agents (e.g., groove binding agents such as minor groove binders), RNA/DNA antimetabolites, cell cycle modulators, kinase inhibitors, protein synthesis inhibitors, histone deacetylase inhibitors, mitochondria inhibitors, and antimetabolic agents.

[0159] Specific non-limiting examples of agents within certain of these various classes are provided below.

[0160] Alkylating Agents: asaley ((L-Leucine, N-[N-acetyl-4-[bis-(2-chloroethyl)amino]-DL-phenylalanyl]-, ethylester; NSC 167780; CAS Registry No. 3577897)); AZQ ((1,4-

cyclohexadiene-1,4-dicarbamic acid, 2,5-bis(1-aziridiny)-3,6-dioxo-, diethyl ester; NSC 182986; CAS Registry No. 57998682); BCNU ((N,N'-Bis(2-chloroethyl)-N-nitrosourea; NSC 409962; CAS Registry No. 154938)); busulfan (1,4-butanediol dimethanesulfonate; NSC 750; CAS Registry No. 55981); (carboxyphthalato)platinum (NSC 27164; CAS Registry No. 65296813); CBDCA ((cis-(1,1-cyclobutanedicarboxylato)diammineplatinum(II)); NSC 241240; CAS Registry No. 41575944); CCNU ((N-(2-chloroethyl)-N'-cyclohexyl-N-nitrosourea; NSC 79037; CAS Registry No. 13010474); CHIP (iproplatin; NSC 256927); chlorambucil (NSC 3088; CAS Registry No. 305033); chlorozotocin ((2-[[[(2-chloroethyl) nitrosoamino]carbonyl]amino]-2-deoxy-D-glucopyranose; NSC 178248; CAS Registry No. 54749905)); cis-platinum (cisplatin; NSC 119875; CAS Registry No. 15663271); clomesone (NSC 338947; CAS Registry No. 88343720); cyanomorpholinodoxorubicin (NCS 357704; CAS Registry No. 88254073); cyclodisone (NSC 348948; CAS Registry No. 99591738); dianhydrogalactitol (5,6-diepoxydulcitol; NSC 132313; CAS Registry No. 23261203); fluorodopan ((5-[(2-chloroethyl)-(2-fluoroethyl)amino]-6-methyl-uracil; NSC 73754; CAS Registry No. 834913); hepsulfam (NSC 329680; CAS Registry No. 96892578); hycanthone (NSC 142982; CAS Registry No. 23255938); melphalan (NSC 8806; CAS Registry No. 3223072); methyl CCNU ((1-(2-chloroethyl)-3-(trans-4-methylcyclohexane)-1-nitrosourea; NSC 95441; 13909096); mitomycin C (NSC 26980; CAS Registry No. 50077); mitozolamide (NSC 353451; CAS Registry No. 85622953); nitrogen mustard ((bis(2-chloroethyl)methylamine hydrochloride; NSC 762; CAS Registry No. 55867); PCNU ((1-(2-chloroethyl)-3-(2,6-dioxo-3-piperidyl)-1-nitrosourea; NSC 95466; CAS Registry No. 13909029)); piperazine alkylator ((1-(2-chloroethyl)-4-(3-chloropropyl)-piperazine dihydrochloride; NSC 344007)); piperazinedione (NSC 135758; CAS Registry No. 41109802); pipobroman ((N,N-bis(3-bromopropionyl) piperazine; NSC 25154; CAS Registry No. 54911)); porfiromycin (N-methylmitomycin C; NSC 56410; CAS Registry No. 801525); spirohydantoin mustard (NSC 172112; CAS Registry No. 56605164); teroxirone (triglycidylisocyanurate; NSC 296934; CAS Registry No. 2451629); tetraplatin (NSC 363812; CAS Registry No. 62816982); thio-tepa (N,N',N''-tri-1,2-ethanediylthio phosphoramidate; NSC 6396; CAS Registry No. 52244); triethylenemelamine (NSC 9706; CAS Registry No. 51183); uracil nitrogen mustard (desmethyldopan; NSC 34462; CAS Registry No. 66751); Yoshi-864 ((bis(3-mesyloxy propyl)amine hydrochloride; NSC 102627; CAS Registry No. 3458228).

[0161] Topoisomerase I Inhibitors: camptothecin (NSC 94600; CAS Registry No. 7689-03-4); various camptothecin derivatives and analogs (for example, NSC 100880, NSC 603071, NSC 107124, NSC 643833, NSC 629971, NSC 295500, NSC 249910, NSC 606985, NSC 74028, NSC 176323, NSC 295501, NSC 606172, NSC 606173, NSC 610458, NSC 618939, NSC 610457, NSC 610459, NSC 606499, NSC 610456, NSC 364830, and NSC 606497); morpholinisoxorubicin (NSC 354646; CAS Registry No. 89196043); SN-38 (NSC 673596; CAS Registry No. 86639-52-3).

[0162] Topoisomerase II Inhibitors: doxorubicin (NSC 123127; CAS Registry No. 25316409); amonafide (benzisoquinolinedione; NSC 308847; CAS Registry No. 69408817); m-AMSA ((4'-(9-acridinylamino)-3'-methoxymethanesulfonanilide; NSC 249992; CAS Registry No. 51264143)); anthrapyrazole derivative ((NSC 355644); etoposide (VP-16; NSC 141540; CAS Registry No. 33419420); pyrazoloacridine ((pyrazolo[3,4,5-kl]acridine-2(6H)-propanamine, 9-methoxy-N, N-dimethyl-5-nitro-, monomethanesulfonate; NSC 366140; CAS Registry No. 99009219); bisantrene hydrochloride (NSC 337766; CAS Registry No. 71439684); daunorubicin (NSC 821151; CAS Registry No. 23541506); deoxydoxorubicin (NSC 267469; CAS Registry No. 63950061); mitoxantrone (NSC 301739; CAS Registry No. 70476823); menogaril (NSC 269148; CAS Registry No. 71628961); N,N-dibenzyl daunomycin (NSC 268242; CAS Registry No. 70878512); oxanthrazole (NSC 349174; CAS Registry No. 105118125); rubidazole (NSC 164011; CAS Registry No. 36508711); teniposide (VM-26; NSC 122819; CAS Registry No. 29767202).

[0163] DNA Intercalating Agents: anthramycin (CAS Registry No. 4803274); chicamycin A (CAS Registry No. 89675376); tomaymycin (CAS Registry No. 35050556); DC-81 (CAS Registry No. 81307246); sibiromycin (CAS Registry No. 12684332); pyrrolobenzodiazepine derivative (CAS Registry No. 945490095); SGD-1882 ((S)-2-(4-aminophenyl)-7-methoxy-8-(3-4(S)-7-methoxy-2-(4-methoxyphenyl)-- 5-oxo-5,11a-dihydro-1H-benzo[e]pyrrolo[1,2-a][1,4]diazepin-8-yl)oxy)propox- y)-1H-benzo[e]pyrrolo[1,2-a][1,4]diazepin-5(11aH)-one); SG2000 (SJG-136; (11aS,11a'S)-8,8'-(propane-1,3-diylbis(oxy))bis(7-methoxy-2-methylene-2,3- -dihydro-1H-benzo[e]pyrrolo[1,2-a][1,4]diazepin-5(11aH)-one); NSC 694501; CAS Registry No. 232931576).

[0164] RNA/DNA Antimetabolites: L-alanosine (NSC 153353; CAS Registry No. 59163416); 5-azacytidine (NSC 102816; CAS Registry No. 320672); 5-fluorouracil (NSC 19893; CAS Registry No. 51218); acivicin (NSC 163501; CAS Registry No. 42228922); aminopterin derivative N-[2-chloro-5-[[[(2,4-diamino-5-methyl-6-quinazolinyl)methyl]amino]benzoyl-]L-aspartic acid (NSC 132483); aminopterin derivative N-[4-[[[(2,4-diamino-5-ethyl-6-quinazolinyl)methyl]amino]benzoyl]L-aspartic acid (NSC 184692); aminopterin derivative N-[2-chloro-4-[[[(2,4-diamino-6-pteridiny]methyl]amino]benzoyl]L-aspartic acid monohydrate (NSC 134033); an antifo ((N^α-(4-amino-4-deoxypteroyl)-N⁷-hemiphthaloyl-L-ornithin- e; NSC 623017)); Baker's soluble antifol (NSC 139105; CAS Registry No. 41191042); dichlorallyl lawsone ((2-(3,3-dichloroallyl)-3-hydroxy-1,4-naphthoquinone; NSC 126771; CAS Registry No. 36417160); brequinar (NSC 368390; CAS Registry No. 96201886); ftorafur ((pro-drug; 5-fluoro-1-(tetrahydro-2-furyl)-uracil; NSC 148958; CAS Registry No. 37076689); 5,6-dihydro-5-azacytidine (NSC 264880; CAS Registry No. 62402317); methotrexate (NSC 740; CAS Registry No. 59052); methotrexate derivative (N-[[4-[[[(2,4-diamino-6-pteridiny]methyl]methylamino]-1-naphthalenyl]car- bonyl]L-glutamic acid; NSC 174121); PALA

((N-(phosphonoacetyl)-L-aspartate; NSC 224131; CAS Registry No. 603425565); pyrazofurin (NSC 143095; CAS Registry No. 30868305); trimetrexate (NSC 352122; CAS Registry No. 82952645).

[0165] DNA Antimetabolites: 3-HP (NSC 95678; CAS Registry No. 3814797); 2'-deoxy-5-fluorouridine (NSC 27640; CAS Registry No. 50919); 5-HP (NSC 107392; CAS Registry No. 19494894); α -TGDR (α -2'-deoxy-6-thioguanosine; NSC 71851 CAS Registry No. 2133815); aphidicolin glycinate (NSC 303812; CAS Registry No. 92802822); ara C (cytosine arabinoside; NSC 63878; CAS Registry No. 69749); 5-aza-2'-deoxycytidine (NSC 127716; CAS Registry No. 2353335); β -TGDR (β -2'-deoxy-6-thioguanosine; NSC 71261; CAS Registry No. 789617); cyclocytidine (NSC 145668; CAS Registry No. 10212256); guanazole (NSC 1895; CAS Registry No. 1455772); hydroxyurea (NSC 32065; CAS Registry No. 127071); inosine glycodialdehyde (NSC 118994; CAS Registry No. 23590990); macbecin II (NSC 330500; CAS Registry No. 73341738); pyrazoloimidazole (NSC 51143; CAS Registry No. 6714290); thioguanine (NSC 752; CAS Registry No. 154427); thiopurine (NSC 755; CAS Registry No. 50442).

[0166] Cell Cycle Modulators: silibinin (CAS Registry No. 22888-70-6); epigallocatechin gallate (EGCG; CAS Registry No. 989515); procyanidin derivatives (e.g., procyanidin A1 [CAS Registry No. 103883030], procyanidin B1 [CAS Registry No. 20315257], procyanidin B4 [CAS Registry No. 29106512], arecatannin B1 [CAS Registry No. 79763283]); isoflavones (e.g., genistein [4%5,7-trihydroxyisoflavone; CAS Registry No. 446720], daidzein [4',7-dihydroxyisoflavone, CAS Registry No. 486668]; indole-3-carbinol (CAS Registry No. 700061); quercetin (NSC 9219; CAS Registry No. 117395); estramustine (NSC 89201; CAS Registry No. 2998574); nocodazole (CAS Registry No. 31430189); podophyllotoxin (CAS Registry No. 518285); vinorelbine tartrate (NSC 608210; CAS Registry No. 125317397); cryptophycin (NSC 667642; CAS Registry No. 124689652).

[0167] Kinase Inhibitors: afatinib (CAS Registry No. 850140726); axitinib (CAS Registry No. 319460850); ARRY-438162 (binimetinib) (CAS Registry No. 606143899); bosutinib (CAS Registry No. 380843754); cabozantinib (CAS Registry No. 1140909483); ceritinib (CAS Registry No. 1032900256); crizotinib (CAS Registry No. 877399525); dabrafenib (CAS Registry No. 1195765457); dasatinib (NSC 732517; CAS Registry No. 302962498); erlotinib (NSC 718781; CAS Registry No. 183319699); everolimus (NSC 733504; CAS Registry No. 159351696); fostamatinib (NSC 745942; CAS Registry No. 901119355); gefitinib (NSC 715055; CAS Registry No. 184475352); ibrutinib (CAS Registry No. 936563961); imatinib (NSC 716051; CAS Registry No. 220127571); lapatinib (CAS Registry No. 388082788); lenvatinib (CAS Registry No. 857890392); mubritinib (CAS 366017096); nilotinib (CAS Registry No. 923288953); nintedanib (CAS Registry No. 656247175); palbociclib (CAS Registry No. 571190302); pazopanib (NSC 737754; CAS Registry No. 635702646); pegaptanib (CAS

Registry No. 222716861); ponatinib (CAS Registry No. 1114544318); rapamycin (NSC 226080; CAS Registry No. 53123889); regorafenib (CAS Registry No. 755037037); AP 23573 (ridaforolimus) (CAS Registry No. 572924540); INCB018424 (ruxolitinib) (CAS Registry No. 1092939177); ARRY-142886 (selumetinib) (NSC 741078; CAS Registry No. 606143-52-6); sirolimus (NSC 226080; CAS Registry No. 53123889); sorafenib (NSC 724772; CAS Registry No. 475207591); sunitinib (NSC 736511; CAS Registry No. 341031547); tofacitinib (CAS Registry No. 477600752); temsirolimus (NSC 683864; CAS Registry No. 163635043); trametinib (CAS Registry No. 871700173); vandetanib (CAS Registry No. 443913733); vemurafenib (CAS Registry No. 918504651); SU6656 (CAS Registry No. 330161870); CEP-701 (lesaurtinib) (CAS Registry No. 111358884); XL019 (CAS Registry No. 945755566); PD-325901 (CAS Registry No. 391210109); PD-98059 (CAS Registry No. 167869218); ATP-competitive TORC1/TORC2 inhibitors including PI-103 (CAS Registry No. 371935749), PP242 (CAS Registry No. 1092351671), PP30 (CAS Registry No. 1092788094), Torin 1 (CAS Registry No. 1222998368), LY294002 (CAS Registry No. 154447366), XL-147 (CAS Registry No. 934526893), CAL-120 (CAS Registry No. 870281348), ETP-45658 (CAS Registry No. 1198357797), PX 866 (CAS Registry No. 502632668), GDC-0941 (CAS Registry No. 957054307), BGT226 (CAS Registry No. 1245537681), BEZ235 (CAS Registry No. 915019657), XL-765 (CAS Registry No. 934493762).

[0168] Protein Synthesis Inhibitors: acriflavine (CAS Registry No. 65589700); amikacin (NSC 177001; CAS Registry No. 39831555); arbekacin (CAS Registry No. 51025855); astromicin (CAS Registry No. 55779061); azithromycin (NSC 643732; CAS Registry No. 83905015); bekanamycin (CAS Registry No. 4696768); chlortetracycline (NSC 13252; CAS Registry No. 64722); clarithromycin (NSC 643733; CAS Registry No. 81103119); clindamycin (CAS Registry No. 18323449); clomocycline (CAS Registry No. 1181540); cycloheximide (CAS Registry No. 66819); dactinomycin (NSC 3053; CAS Registry No. 50760); dalfopristin (CAS Registry No. 112362502); demeclocycline (CAS Registry No. 127333); dibekacin (CAS Registry No. 34493986); dihydrostreptomycin (CAS Registry No. 128461); dirithromycin (CAS Registry No. 62013041); doxycycline (CAS Registry No. 17086281); emetine (NSC 33669; CAS Registry No. 483181); erythromycin (NSC 55929; CAS Registry No. 114078); flurithromycin (CAS Registry No. 83664208); framycetin (neomycin B; CAS Registry No. 119040); gentamycin (NSC 82261; CAS Registry No. 1403663); glycylicyclines, such as tigecycline (CAS Registry No. 220620097); hygromycin B (CAS Registry No. 31282049); isepamicin (CAS Registry No. 67814760); josamycin (NSC 122223; CAS Registry No. 16846245); kanamycin (CAS Registry No. 8063078); ketolides such as telithromycin (CAS Registry No. 191114484), cethromycin (CAS Registry No. 205110481), and solithromycin (CAS Registry No. 760981837); lincomycin (CAS Registry No. 154212); lymecycline (CAS Registry No. 992212); meclocycline (NSC 78502; CAS Registry No. 2013583); metacycline (rondomycin; NSC 356463; CAS Registry No. 914001); midecamycin (CAS Registry No. 35457808); minocycline (NSC 141993; CAS Registry No.

10118908); miocamycin (CAS Registry No. 55881077); neomycin (CAS Registry No. 119040); netilmicin (CAS Registry No. 56391561); oleandomycin (CAS Registry No. 3922905); oxazolidinones, such as eperezolid (CAS Registry No. 165800044), linezolid (CAS Registry No. 165800033), posizolid (CAS Registry No. 252260029), radezolid (CAS Registry No. 869884786), ranbezolid (CAS Registry No. 392659380), sutezolid (CAS Registry No. 168828588), tedizolid (CAS Registry No. 856867555); oxytetracycline (NSC 9169; CAS Registry No. 2058460); paromomycin (CAS Registry No. 7542372); penimepicycline (CAS Registry No. 4599604); peptidyl transferase inhibitors, e.g., chloramphenicol (NSC 3069; CAS Registry No. 56757) and derivatives such as azidamfenicol (CAS Registry No. 13838089), florfenicol (CAS Registry No. 73231342), and thiamphenicol (CAS Registry No. 15318453), and pleuromutilins such as retapamulin (CAS Registry No. 224452668), tiamulin (CAS Registry No. 55297955), valnemulin (CAS Registry No. 101312929); pirlimycin (CAS Registry No. 79548735); puromycin (NSC 3055; CAS Registry No. 53792); quinupristin (CAS Registry No. 120138503); ribostamycin (CAS Registry No. 53797356); rokitamycin (CAS Registry No. 74014510); rolitetracycline (CAS Registry No. 751973); roxithromycin (CAS Registry No. 80214831); sisomicin (CAS Registry No. 32385118); spectinomycin (CAS Registry No. 1695778); spiramycin (CAS Registry No. 8025818); streptogramins such as pristnamycin (CAS Registry No. 270076603), quinupristin/dalfopristin (CAS Registry No. 126602899), and virginiamycin (CAS Registry No. 11006761); streptomycin (CAS Registry No. 57921); tetracycline (NSC 108579; CAS Registry No. 60548); tobramycin (CAS Registry No. 32986564); troleandomycin (CAS Registry No. 2751099); tylosin (CAS Registry No. 1401690); verdamicin (CAS Registry No. 49863481).

[0169] Histone Deacetylase Inhibitors: abexinostat (CAS Registry No. 783355602); belinostat (NSC 726630; CAS Registry No. 414864009); chidamide (CAS Registry No. 743420022); entinostat (CAS Registry No. 209783802); givinostat (CAS Registry No. 732302997); mocetinostat (CAS Registry No. 726169739); panobinostat (CAS Registry No. 404950807); quisinostat (CAS Registry No. 875320299); resminostat (CAS Registry No. 864814880); romidepsin (CAS Registry No. 128517077); sulforaphane (CAS Registry No. 4478937); thioureaobutyronitrile (Kevetrin™; CAS Registry No. 6659890); valproic acid (NSC 93819; CAS Registry No. 99661); vorinostat (NSC 701852; CAS Registry No. 149647789); ACY-1215 (rocilinostat; CAS Registry No. 1316214524); CUDC-101 (CAS Registry No. 1012054599); CHR-2845 (tefinostat; CAS Registry No. 914382608); CHR-3996 (CAS Registry No. 1235859138); 4SC-202 (CAS Registry No. 910462430); CG200745 (CAS Registry No. 936221339); SB939 (pracinostat; CAS Registry No. 929016966).

[0170] Mitochondria Inhibitors: pancratistatin (NSC 349156; CAS Registry No. 96281311); rhodamine-123 (CAS Registry No. 63669709); edelfosine (NSC 324368; CAS Registry No. 70641519); d-alpha-tocopherol succinate (NSC 173849; CAS Registry No. 4345033);

compound 11 β (CAS Registry No. 865070377); aspirin (NSC 406186; CAS Registry No. 50782); ellipticine (CAS Registry No. 519233); berberine (CAS Registry No. 633658); cerulenin (CAS Registry No. 17397896); GX015-070 (Obatoclox®; 1H-Indole, 2-(2-((3,5-dimethyl-1H-pyrrol-2-yl)methylene)-3-methoxy-2H-pyrrol-5-yl)-; NSC 729280; CAS Registry No. 803712676); celastrol (tripterine; CAS Registry No. 34157830); metformin (NSC 91485; CAS Registry No. 1115704); Brilliant green (NSC 5011; CAS Registry No. 633034); ME-344 (CAS Registry No. 1374524556).

[0171] Antimitotic Agents: allocolchicine (NSC 406042); auristatins, such as MMAE (monomethyl auristatin E; CAS Registry No. 474645-27-7) and MMAF (monomethyl auristatin F; CAS Registry No. 745017-94-1; halichondrin B (NSC 609395); colchicine (NSC 757; CAS Registry No. 64868); colchicine derivative (N-benzoyl-deacetyl benzamide; NSC 33410; CAS Registry No. 63989753); dolastatin 10 (NSC 376128; CAS Registry No. 110417-88-4); maytansine (NSC 153858; CAS Registry No. 35846-53-8); rhoxoxin (NSC 332598; CAS Registry No. 90996546); taxol (NSC 125973; CAS Registry No. 33069624); taxol derivative ((2'-N-[3-(dimethylamino)propyl]glutaramate taxol; NSC 608832); thiocolchicine (3-demethylthiocolchicine; NSC 361792); trityl cysteine (NSC 49842; CAS Registry No. 2799077); vinblastine sulfate (NSC 49842; CAS Registry No. 143679); vincristine sulfate (NSC 67574; CAS Registry No. 2068782).

[0172] Any of these agents that include or that may be modified to include a site of attachment to an antibody may be included in the ADCs disclosed herein.

[0173] In a specific embodiment, the cytotoxic and/or cytostatic agent is an antimitotic agent.

[0174] In another specific embodiment, the cytotoxic and/or cytostatic agent is an auristatin, for example, monomethyl auristatin E ("MMAE") or monomethyl auristatin F ("MMAF").

5.2.2. Linkers

[0175] In the anti-glyco-LAMP1 ADCs of the disclosure, the cytotoxic and/or cytostatic agents are linked to the antibody by way of linkers. The linker linking a cytotoxic and/or cytostatic agent to the antibody of an ADC may be short, long, hydrophobic, hydrophilic, flexible or rigid, or may be composed of segments that each independently have one or more of the above-mentioned properties such that the linker may include segments having different properties. The linkers may be polyvalent such that they covalently link more than one agent to a single site on the antibody, or monovalent such that covalently they link a single agent to a single site on the antibody.

[0176] As will be appreciated by skilled artisans, the linkers link cytotoxic and/or cytostatic agents to the antibody by forming a covalent linkage to the cytotoxic and/or cytostatic agent at one location and a covalent linkage to antibody at another. The covalent linkages are formed by reaction between functional groups on the linker and functional groups on the agents and

antibody. As used herein, the expression "linker" is intended to include (i) unconjugated forms of the linker that include a functional group capable of covalently linking the linker to a cytotoxic and/or cytostatic agent and a functional group capable of covalently linking the linker to an antibody; (ii) partially conjugated forms of the linker that includes a functional group capable of covalently linking the linker to an antibody and that is covalently linked to a cytotoxic and/or cytostatic agent, or vice versa; and (iii) fully conjugated forms of the linker that is covalently linked to both a cytotoxic and/or cytostatic agent and an antibody. In some specific embodiments of linkers and anti-glyco-LAMP1 ADCs of the disclosure, as well as synthons used to conjugate linker-agents to antibodies, moieties comprising the functional groups on the linker and covalent linkages formed between the linker and antibody are specifically illustrated as R_x and XY, respectively.

[0177] The linkers are preferably, but need not be, chemically stable to conditions outside the cell, and may be designed to cleave, immolate and/or otherwise specifically degrade inside the cell. Alternatively, linkers that are not designed to specifically cleave or degrade inside the cell may be used. Choice of stable versus unstable linker may depend upon the toxicity of the cytotoxic and/or cytostatic agent. For agents that are toxic to normal cells, stable linkers are preferred. Agents that are selective or targeted and have lower toxicity to normal cells may utilize, chemical stability of the linker to the extracellular milieu is less important. A wide variety of linkers useful for linking drugs to antibodies in the context of ADCs are known in the art. Any of these linkers, as well as other linkers, may be used to link the cytotoxic and/or cytostatic agents to the antibody of the anti-glyco-LAMP1 ADCs of the disclosure.

[0178] Exemplary polyvalent linkers that may be used to link many cytotoxic and/or cytostatic agents to a single antibody molecule are described, for example, in WO 2009/073445; WO 2010/068795; WO 2010/138719; WO 2011/120053; WO 2011/171020; WO 2013/096901; WO 2014/008375; WO 2014/093379; WO 2014/093394; WO 2014/093640, the content of which are incorporated herein by reference in their entireties. For example, the Fleximer linker technology developed by Mersana *et al.* has the potential to enable high-DAR ADCs with good physicochemical properties. As shown below, the Mersana technology is based on incorporating drug molecules into a solubilizing poly-acetal backbone via a sequence of ester bonds. The methodology renders highly-loaded ADCs (DAR up to 20) while maintaining good physicochemical properties.

[0179] Additional examples of dendritic type linkers can be found in US 2006/116422; US 2005/271615; de Groot *et al.* (2003) *Angew. Chem. Int. Ed.* 42:4490-4494; Amir *et al.* (2003) *Angew. Chem. Int. Ed.* 42:4494-4499; Shamis *et al.* (2004) *J. Am. Chem. Soc.* 126:1726-1731; Sun *et al.* (2002) *Bioorganic & Medicinal Chemistry Letters* 12:2213-2215; Sun *et al.* (2003) *Bioorganic & Medicinal Chemistry* 11:1761-1768; King *et al.* (2002) *Tetrahedron Letters* 43:1987-1990, each of which is incorporated herein by reference.

[0180] Exemplary monovalent linkers that may be used are described, for example, in Nolting, 2013, Antibody-Drug Conjugates, Methods in Molecular Biology 1045:71-100; Kitson *et al.*, 2013, CROs/CMOs--Chemica Oggi--Chemistry Today 31(4):30-38; Ducry *et al.*, 2010, Bioconjugate Chem. 21:5-13; Zhao *et al.*, 2011, J. Med. Chem. 54:3606-3623; U.S. Pat. No. 7,223,837; U.S. Pat. No. 8,568,728; U.S. Pat. No. 8,535,678; and WO2004010957, each of which is incorporated herein by reference.

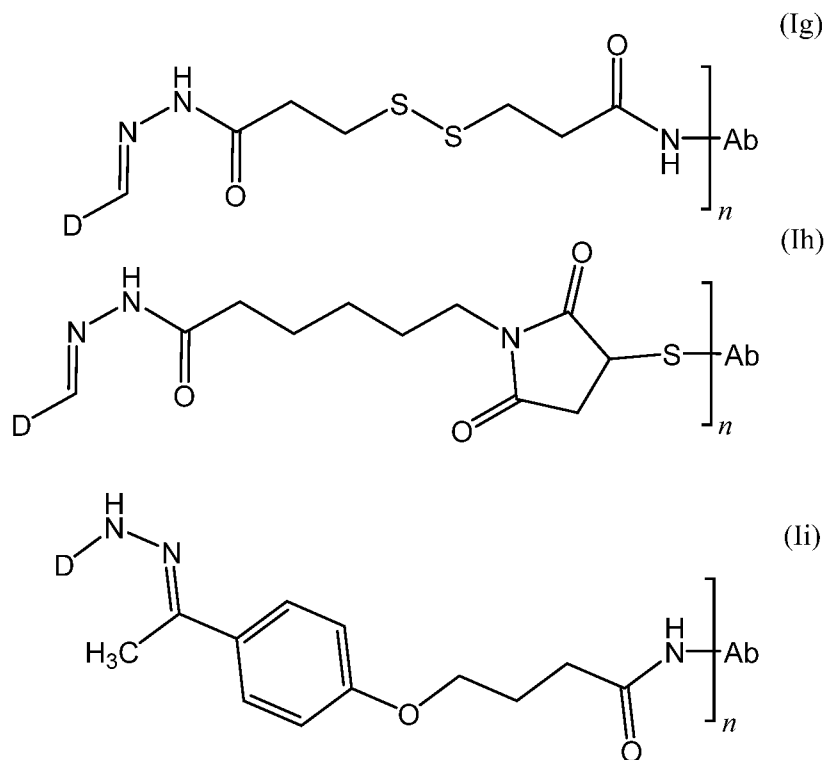
[0181] By way of example and not limitation, some cleavable and noncleavable linkers that may be included in the anti-glyco-LAMP1 ADCs of the disclosure are described below.

5.2.3. Cleavable Linkers

[0182] In certain embodiments, the linker selected is cleavable *in vivo*. Cleavable linkers may include chemically or enzymatically unstable or degradable linkages. Cleavable linkers generally rely on processes inside the cell to liberate the drug, such as reduction in the cytoplasm, exposure to acidic conditions in the lysosome, or cleavage by specific proteases or other enzymes within the cell. Cleavable linkers generally incorporate one or more chemical bonds that are either chemically or enzymatically cleavable while the remainder of the linker is noncleavable. In certain embodiments, a linker comprises a chemically labile group such as hydrazone and/or disulfide groups. Linkers comprising chemically labile groups exploit differential properties between the plasma and some cytoplasmic compartments. The intracellular conditions to facilitate drug release for hydrazone containing linkers are the acidic environment of endosomes and lysosomes, while the disulfide containing linkers are reduced in the cytosol, which contains high thiol concentrations, *e.g.*, glutathione. In certain embodiments, the plasma stability of a linker comprising a chemically labile group may be increased by introducing steric hindrance using substituents near the chemically labile group.

[0183] Acid-labile groups, such as hydrazone, remain intact during systemic circulation in the blood's neutral pH environment (pH 7.3-7.5) and undergo hydrolysis and release the drug once the ADC is internalized into mildly acidic endosomal (pH 5.0-6.5) and lysosomal (pH 4.5-5.0) compartments of the cell. This pH dependent release mechanism has been associated with nonspecific release of the drug. To increase the stability of the hydrazone group of the linker, the linker may be varied by chemical modification, *e.g.*, substitution, allowing tuning to achieve more efficient release in the lysosome with a minimized loss in circulation.

[0184] Hydrazone-containing linkers may contain additional cleavage sites, such as additional acid-labile cleavage sites and/or enzymatically labile cleavage sites. ADCs including exemplary hydrazone-containing linkers include the following structures:



wherein D and Ab represent the cytotoxic and/or cytostatic agent (drug) and Ab, respectively, and n represents the number of drug-linkers linked to the antibody. In certain linkers such as linker (Ig), the linker comprises two cleavable groups--a disulfide and a hydrazone moiety. For such linkers, effective release of the unmodified free drug requires acidic pH or disulfide reduction and acidic pH. Linkers such as (Ih) and (Ii) have been shown to be effective with a single hydrazone cleavage site.

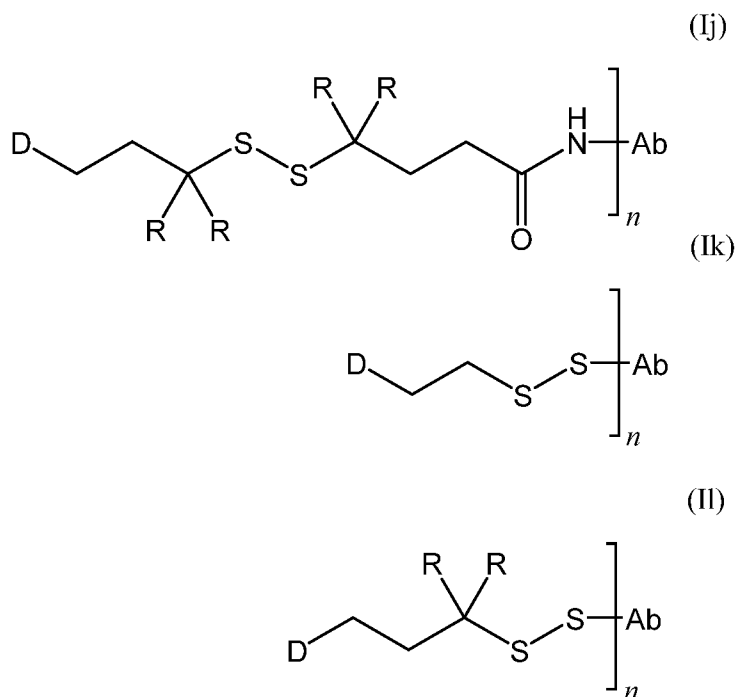
[0185] Additional linkers which remain intact during systemic circulation and undergo hydrolysis and release the drug when the ADC is internalized into acidic cellular compartments include carbonates. Such linkers can be useful in cases where the cytotoxic and/or cytostatic agent can be covalently attached through an oxygen.

[0186] Other acid-labile groups that may be included in linkers include cis-aconityl-containing linkers. cis-Aconityl chemistry uses a carboxylic acid juxtaposed to an amide bond to accelerate amide hydrolysis under acidic conditions.

[0187] Cleavable linkers may also include a disulfide group. Disulfides are thermodynamically stable at physiological pH and are designed to release the drug upon internalization inside cells, wherein the cytosol provides a significantly more reducing environment compared to the extracellular environment. Scission of disulfide bonds generally requires the presence of a cytoplasmic thiol cofactor, such as (reduced) glutathione (GSH), such that disulfide-containing linkers are reasonably stable in circulation, selectively releasing the drug in the cytosol. The intracellular enzyme protein disulfide isomerase, or similar enzymes capable of cleaving

disulfide bonds, may also contribute to the preferential cleavage of disulfide bonds inside cells. GSH is reported to be present in cells in the concentration range of 0.5-10 mM compared with a significantly lower concentration of GSH or cysteine, the most abundant low-molecular weight thiol, in circulation at approximately 5 Tumor cells, where irregular blood flow leads to a hypoxic state, result in enhanced activity of reductive enzymes and therefore even higher glutathione concentrations. In certain embodiments, the *in vivo* stability of a disulfide-containing linker may be enhanced by chemical modification of the linker, e.g., use of steric hindrance adjacent to the disulfide bond.

[0188] ADCs including exemplary disulfide-containing linkers include the following structures:



wherein D and Ab represent the drug and antibody, respectively, n represents the number of drug-linkers linked to the antibody and R is independently selected at each occurrence from hydrogen or alkyl, for example. In certain embodiments, increasing steric hindrance adjacent to the disulfide bond increases the stability of the linker. Structures such as (Ij) and (II) show increased *in vivo* stability when one or more R groups is selected from a lower alkyl such as methyl.

[0189] Another type of cleavable linker that may be used is a linker that is specifically cleaved by an enzyme. Such linkers are typically peptide-based or include peptidic regions that act as substrates for enzymes. Peptide based linkers tend to be more stable in plasma and extracellular milieu than chemically labile linkers. Peptide bonds generally have good serum stability, as lysosomal proteolytic enzymes have very low activity in blood due to endogenous inhibitors and the unfavorably high pH value of blood compared to lysosomes. Release of a drug from an antibody occurs specifically due to the action of lysosomal proteases, e.g.,

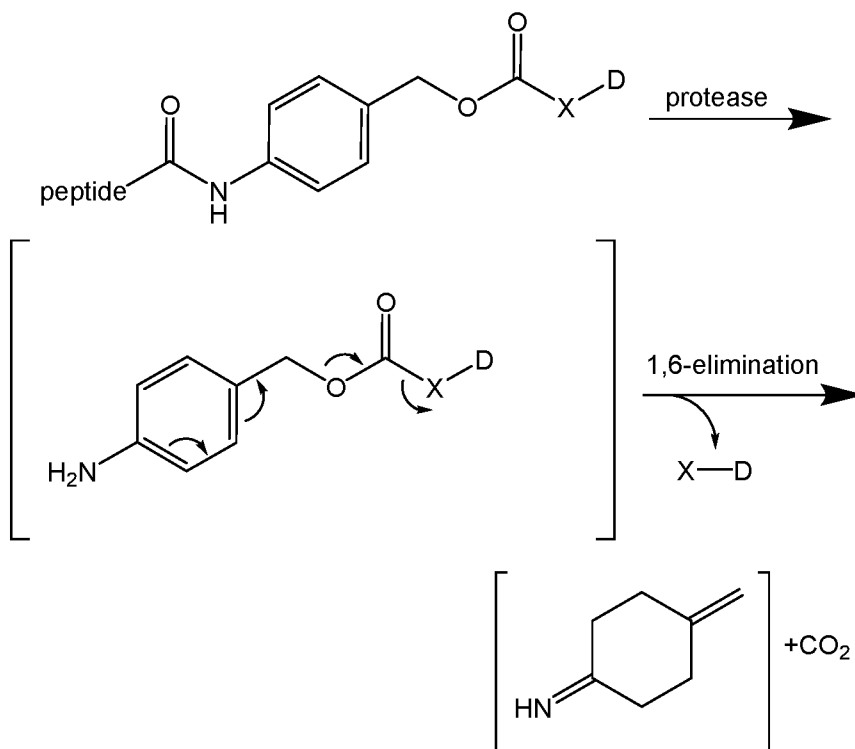
cathepsin and plasmin. These proteases may be present at elevated levels in certain tumor cells.

[0190] In exemplary embodiments, the cleavable peptide is selected from tetrapeptides such as Gly-Phe-Leu-Gly (SEQ ID NO:157), Ala-Leu-Ala-Leu (SEQ ID NO:158) or dipeptides such as Val-Cit, Val-Ala, Met-(D)Lys, Asn-(D)Lys, Val-(D)Asp, Phe-Lys, Ile-Val, Asp-Val, His-Val, NorVal-(D)Asp, Ala-(D)Asp 5, Met-Lys, Asn-Lys, Ile-Pro, Me3Lys-Pro, PhenylGly-(D)Lys, Met-(D)Lys, Asn-(D)Lys, Pro-(D)Lys, Met-(D)Lys, Asn-(D)Lys, AM Met-(D)Lys, Asn-(D)Lys, AW Met-(D)Lys, and Asn-(D)Lys. In certain embodiments, dipeptides are preferred over longer polypeptides due to hydrophobicity of the longer peptides.

[0191] A variety of dipeptide-based cleavable linkers useful for linking drugs such as doxorubicin, mitomycin, camptothecin, pyrrolobenzodiazepine, tallysomycin and auristatin/auristatin family members to antibodies have been described (see, Dubowchik *et al.*, 1998, J. Org. Chem. 67:1866-1872; Dubowchik *et al.*, 1998, Bioorg. Med. Chem. Lett. 8(21):3341-3346; Walker *et al.*, 2002, Bioorg. Med. Chem. Lett. 12:217-219; Walker *et al.*, 2004, Bioorg. Med. Chem. Lett. 14:4323-4327; Sutherland *et al.*, 2013, Blood 122: 1455-1463; and Francisco *et al.*, 2003, Blood 102:1458-1465, of each of which is incorporated herein by reference). All of these dipeptide linkers, or modified versions of these dipeptide linkers, may be used in the anti-glyco-LAMP1 ADCs of the disclosure. Other dipeptide linkers that may be used include those found in ADCs such as Seattle Genetics' Brentuximab Vendotin SGN-35 (Adcetris™), Seattle Genetics SGN-75 (anti-CD-70, Val-Cit-monomethyl auristatin F(MMAF), Seattle Genetics SGN-CD33A (anti-CD-33, Val-Ala-(SGD-1882)), Celldex Therapeutics glembatumumab (CDX-011) (anti-NMB, Val-Cit-monomethyl auristatin E (MMAE), and Cytogen PSMA-ADC (PSMA-ADC-1301) (anti-PSMA, Val-Cit-MMAE).

[0192] Enzymatically cleavable linkers may include a self-immolative spacer to spatially separate the drug from the site of enzymatic cleavage. The direct attachment of a drug to a peptide linker can result in proteolytic release of an amino acid adduct of the drug, thereby impairing its activity. The use of a self-immolative spacer allows for the elimination of the fully active, chemically unmodified drug upon amide bond hydrolysis.

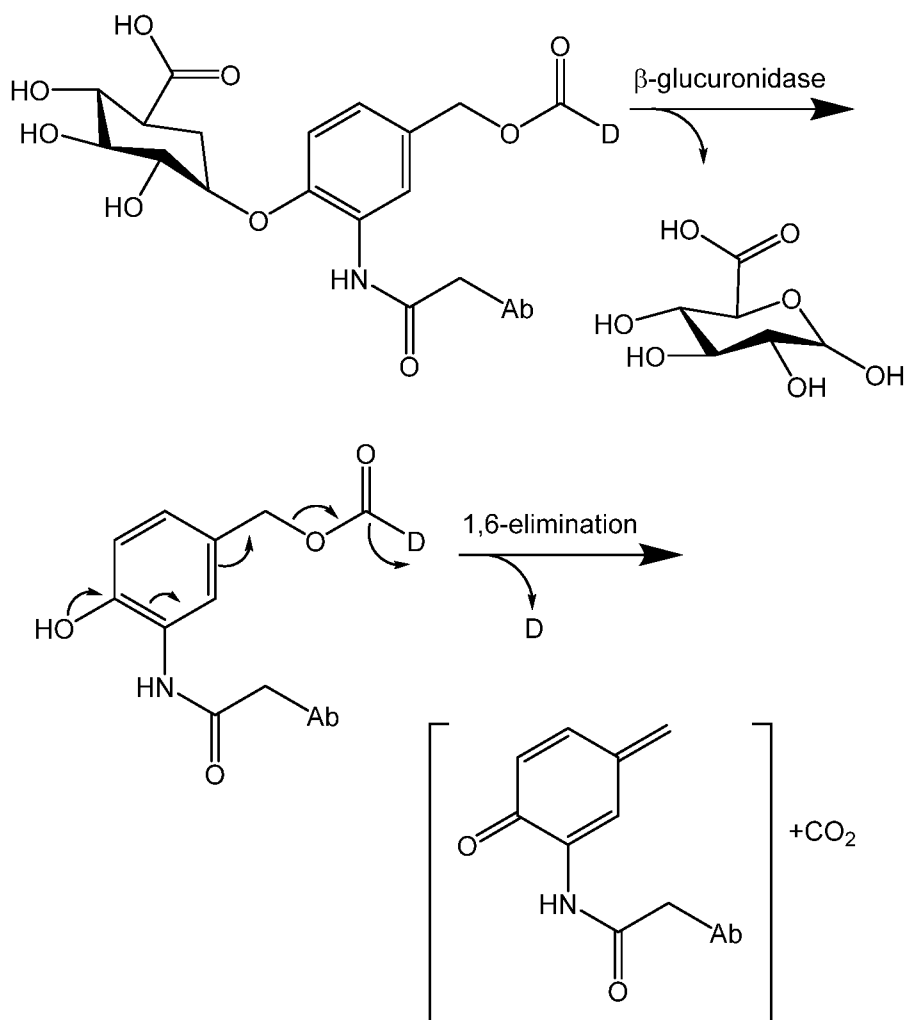
[0193] One self-immolative spacer is the bifunctional para-aminobenzyl alcohol group, which is linked to the peptide through the amino group, forming an amide bond, while amine containing drugs may be attached through carbamate functionalities to the benzylic hydroxyl group of the linker (PABC). The resulting prodrugs are activated upon protease-mediated cleavage, leading to a 1,6-elimination reaction releasing the unmodified drug, carbon dioxide, and remnants of the linker group. The following scheme depicts the fragmentation of p-amidobenzyl ether and release of the drug:



wherein X-D represents the unmodified drug.

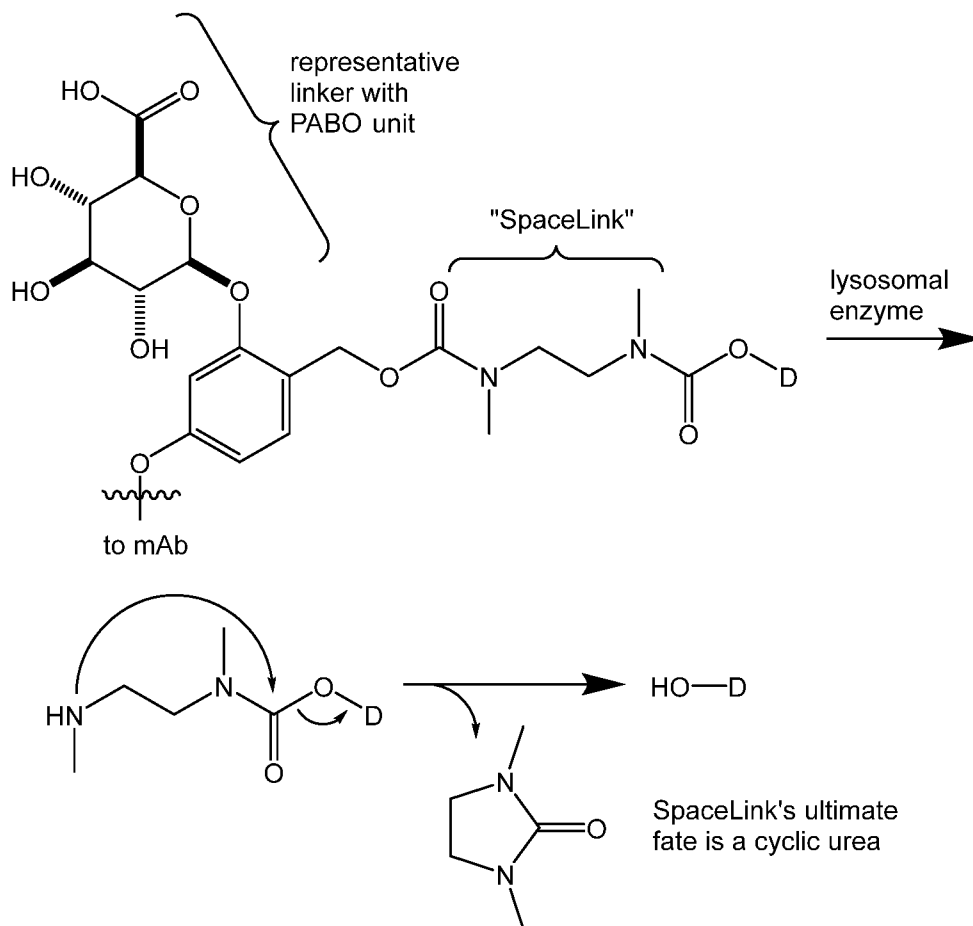
[0194] Heterocyclic variants of this self-immolative group have also been described. See for example, U.S. Pat. No. 7,989,434, incorporated herein by reference.

[0195] In some embodiments, the enzymatically cleavable linker is a β -glucuronic acid-based linker. Facile release of the drug may be realized through cleavage of the β -glucuronide glycosidic bond by the lysosomal enzyme β -glucuronidase. This enzyme is present abundantly within lysosomes and is overexpressed in some tumor types, while the enzyme activity outside cells is low. β -Glucuronic acid-based linkers may be used to circumvent the tendency of an ADC to undergo aggregation due to the hydrophilic nature of β -glucuronides. In some embodiments, β -glucuronic acid-based linkers are preferred as linkers for ADCs linked to hydrophobic drugs. The following scheme depicts the release of the drug from an ADC containing a β -glucuronic acid-based linker:



[0196] A variety of cleavable β -glucuronic acid-based linkers useful for linking drugs such as auristatins, camptothecin and doxorubicin analogues, CBI minor-groove binders, and psymberin to antibodies have been described (see, see Nolting, Chapter 5 "Linker Technology in Antibody-Drug Conjugates," In: Antibody-Drug Conjugates: Methods in Molecular Biology, vol. 1045, pp. 71-100, Laurent Ducry (Ed.), Springer Science & Business Media, LLC, 2013; Jeffrey *et al.*, 2006, Bioconjug. Chem. 17:831-840; Jeffrey *et al.*, 2007, Bioorg. Med. Chem. Lett. 17:2278-2280; and Jiang *et al.*, 2005, J. Am. Chem. Soc. 127:11254-11255, each of which is incorporated herein by reference). All of these β -glucuronic acid-based linkers may be used in the anti-glyco-LAMP1 ADCs of the disclosure.

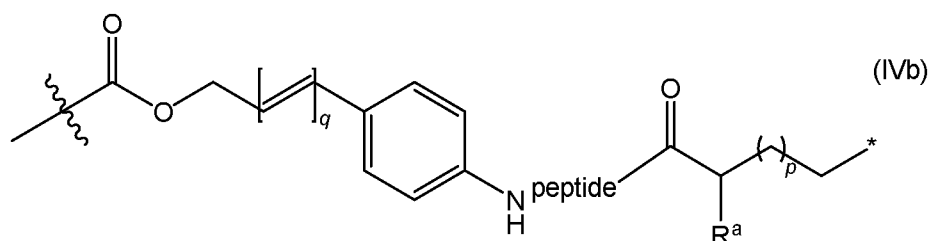
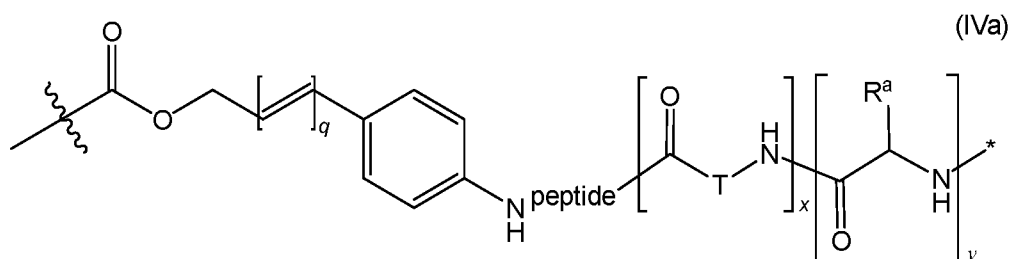
[0197] Additionally, cytotoxic and/or cytostatic agents containing a phenol group can be covalently bonded to a linker through the phenolic oxygen. One such linker, described in WO 2007/089149, relies on a methodology in which a diamino-ethane "SpaceLink" is used in conjunction with traditional "PABO"-based self-immolative groups to deliver phenols. The cleavage of the linker is depicted schematically below, where D represents a cytotoxic and/or cytostatic agent having a phenolic hydroxyl group.



[0198] Cleavable linkers may include noncleavable portions or segments, and/or cleavable segments or portions may be included in an otherwise non-cleavable linker to render it cleavable. By way of example only, polyethylene glycol (PEG) and related polymers may include cleavable groups in the polymer backbone. For example, a polyethylene glycol or polymer linker may include one or more cleavable groups such as a disulfide, a hydrazone or a dipeptide.

[0199] Other degradable linkages that may be included in linkers include ester linkages formed by the reaction of PEG carboxylic acids or activated PEG carboxylic acids with alcohol groups on a biologically active agent, wherein such ester groups generally hydrolyze under physiological conditions to release the biologically active agent. Hydrolytically degradable linkages include, but are not limited to, carbonate linkages; imine linkages resulting from reaction of an amine and an aldehyde; phosphate ester linkages formed by reacting an alcohol with a phosphate group; acetal linkages that are the reaction product of an aldehyde and an alcohol; orthoester linkages that are the reaction product of a formate and an alcohol; and oligonucleotide linkages formed by a phosphoramidite group, including but not limited to, at the end of a polymer, and a 5' hydroxyl group of an oligonucleotide.

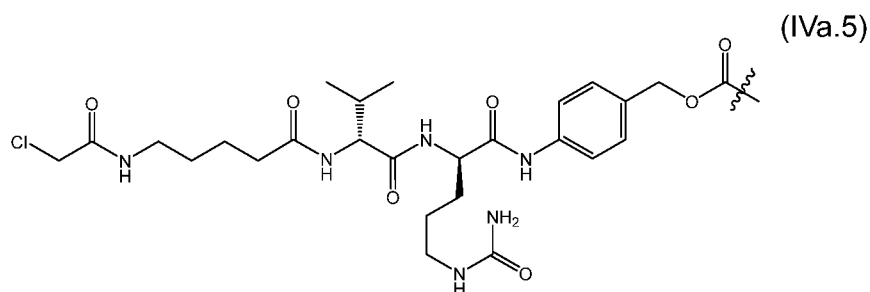
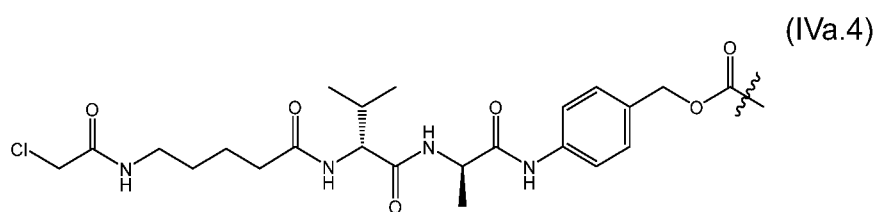
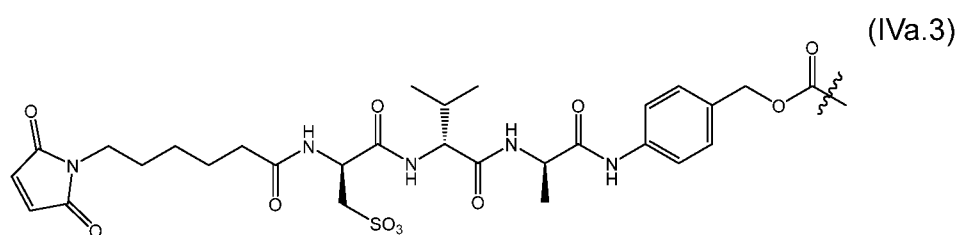
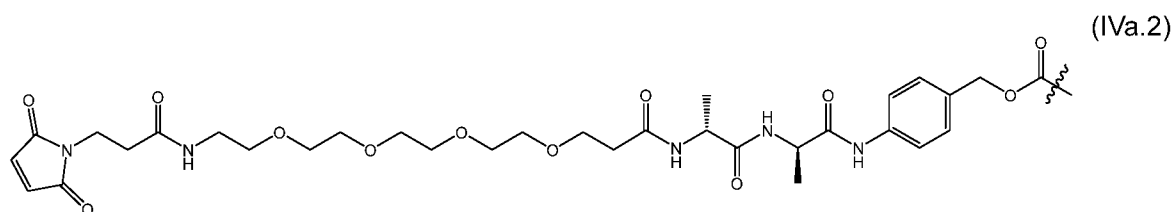
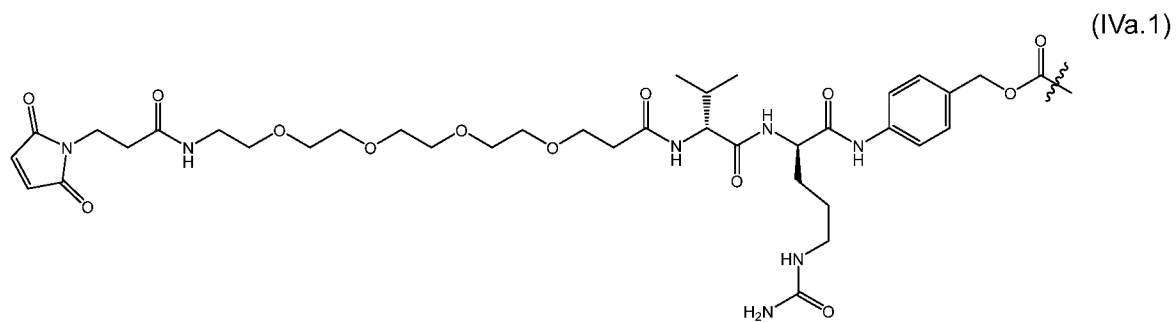
[0200] In certain embodiments, the linker comprises an enzymatically cleavable peptide moiety, for example, a linker comprising structural formula (IVa) or (IVb):

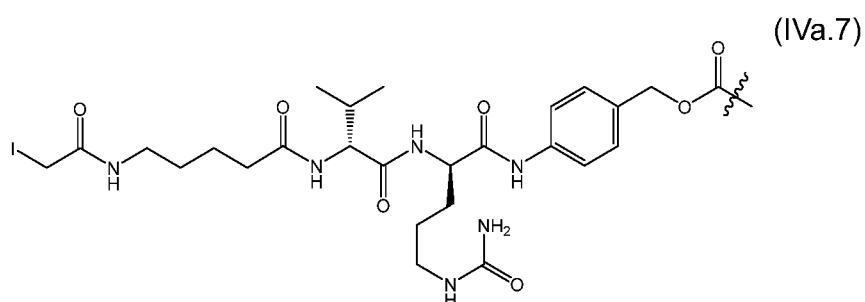
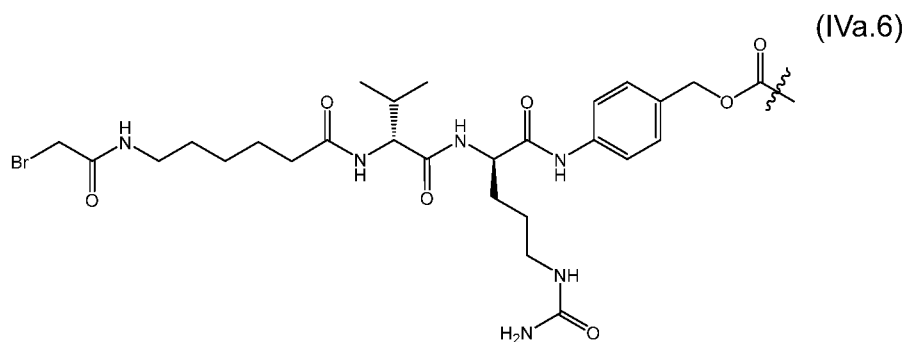


or a salt thereof, wherein: peptide represents a peptide (illustrated C→N and not showing the carboxy and amino “termini”) cleavable by a lysosomal enzyme; T represents a polymer comprising one or more ethylene glycol units or an alkylene chain, or combinations thereof; R^a is selected from hydrogen, alkyl, sulfonate and methyl sulfonate; p is an integer ranging from 0 to 5; q is 0 or 1; x is 0 or 1; y is 0 or 1; represents the point of attachment of the linker to a cytotoxic and/or cytostatic agent; and * represents the point of attachment to the remainder of the linker.

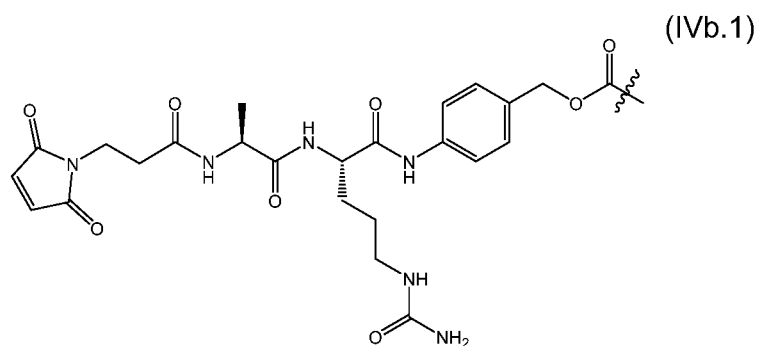
[0201] In certain embodiments, the peptide is selected from a tripeptide or a dipeptide. In particular embodiments, the dipeptide is selected from: Val-Cit; Cit-Val; Ala-Ala; Ala-Cit; Cit-Ala; Asn-Cit; Cit-Asn; Cit-Cit; Val-Glu; Glu-Val; Ser-Cit; Cit-Ser; Lys-Cit; Cit-Lys; Asp-Cit; Cit-Asp; Ala-Val; Val-Ala; Phe-Lys; Val-Lys; Ala-Lys; Phe-Cit; Leu-Cit; Ile-Cit; Phe-Arg; and Trp-Cit. In certain embodiments, the dipeptide is selected from: Cit-Val; and Ala-Val.

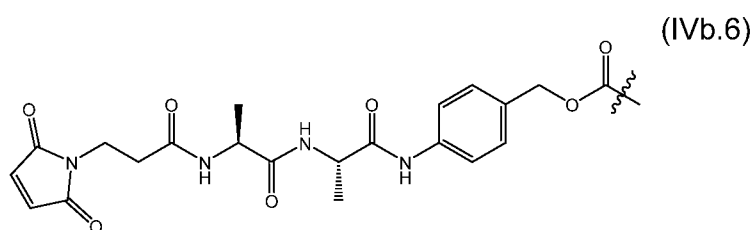
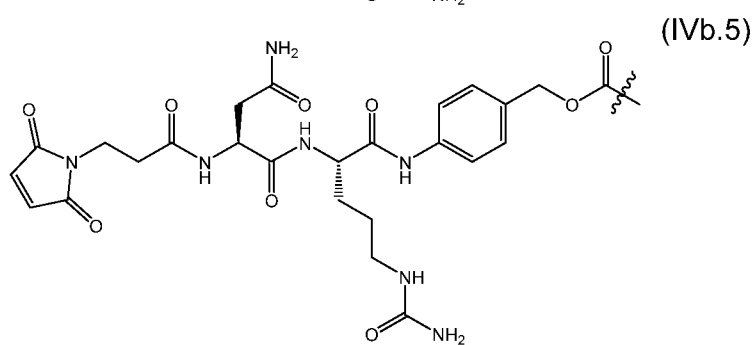
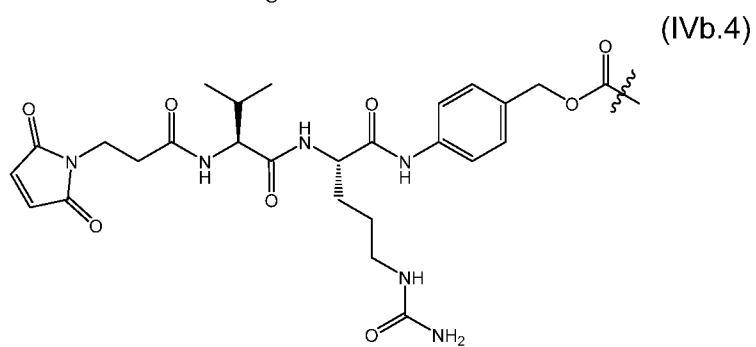
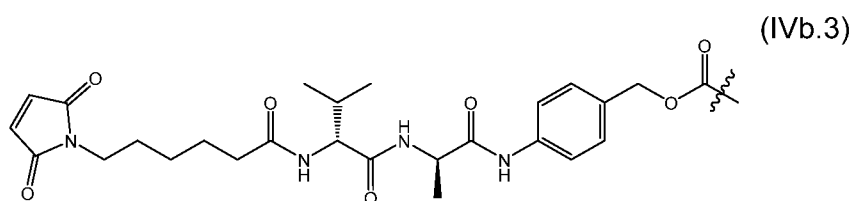
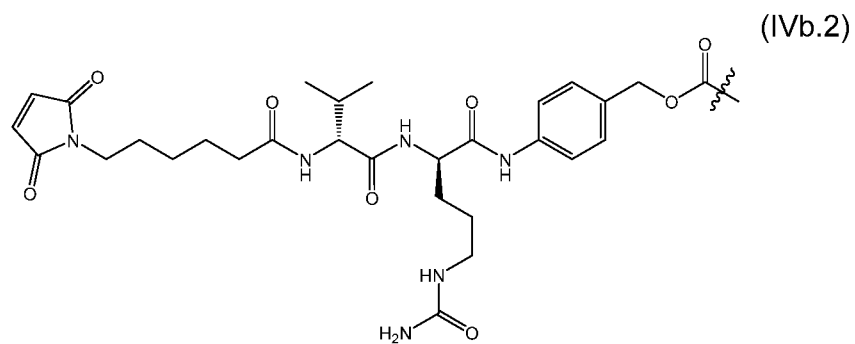
[0202] Specific exemplary embodiments of linkers according to structural formula (IVa) that may be included in the anti-glyco-LAMP1 ADCs of the disclosure include the linkers illustrated below (as illustrated, the linkers include a group suitable for covalently linking the linker to an antibody):

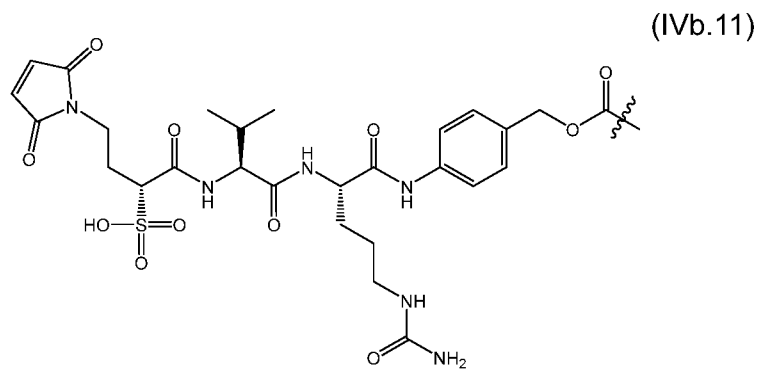
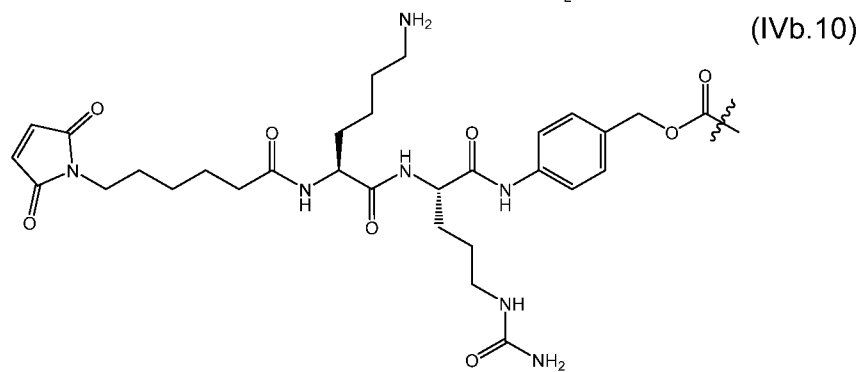
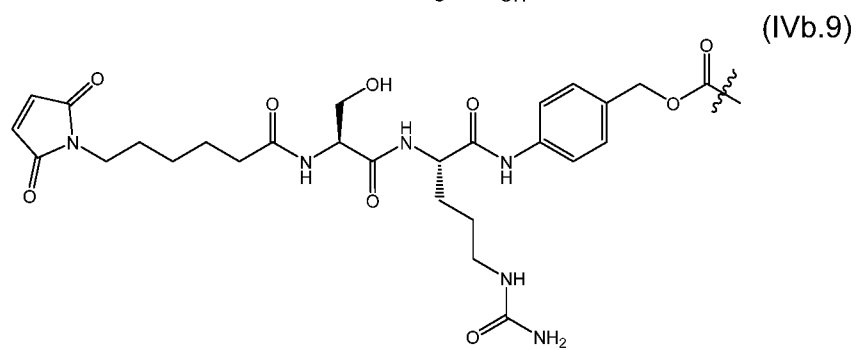
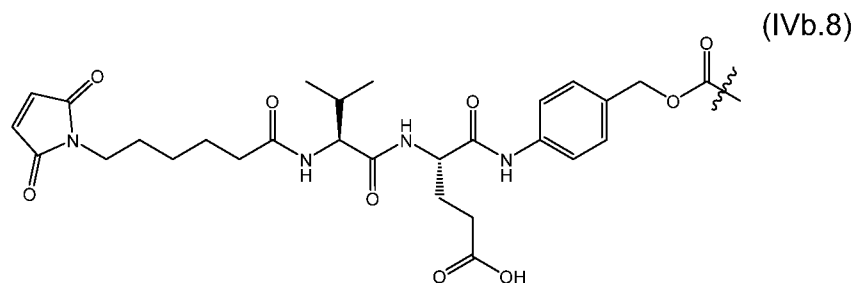
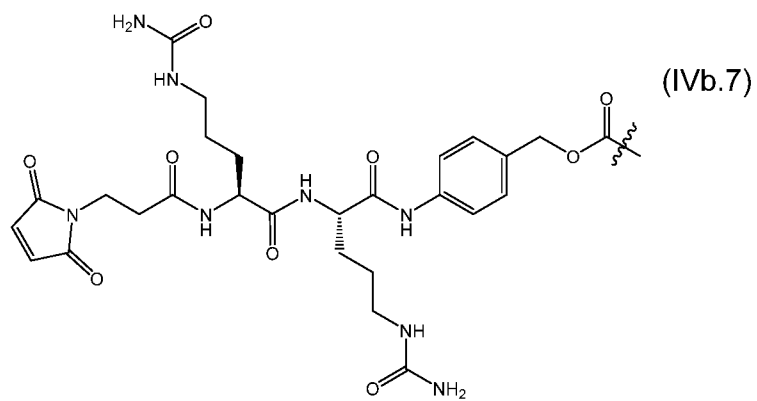




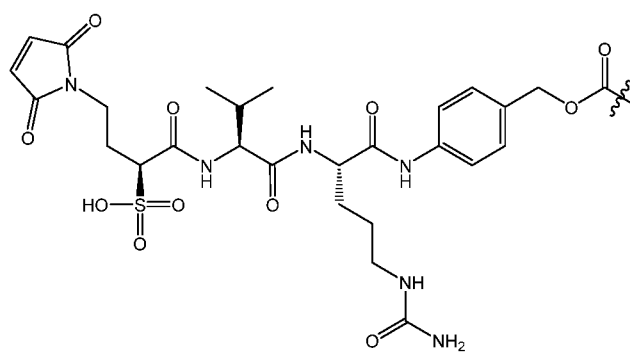
[0203] Specific exemplary embodiments of linkers according to structural formula (IVb) that may be included in the anti-glyco-LAMP1 ADCs of the disclosure include the linkers illustrated below (as illustrated, the linkers include a group suitable for covalently linking the linker to an antibody):



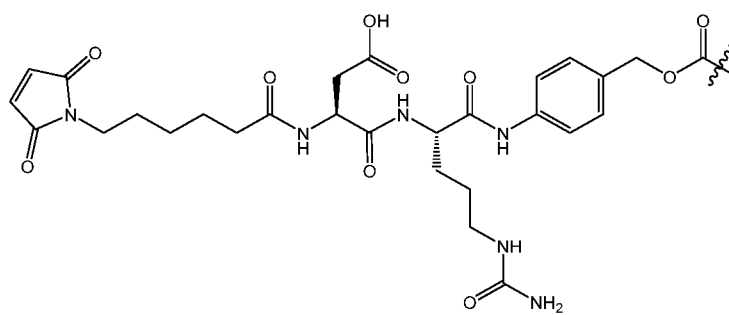




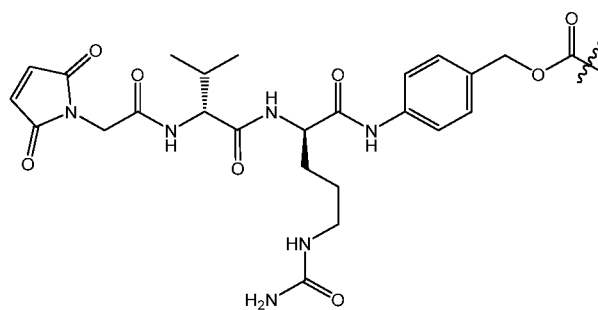
(IVb.12)



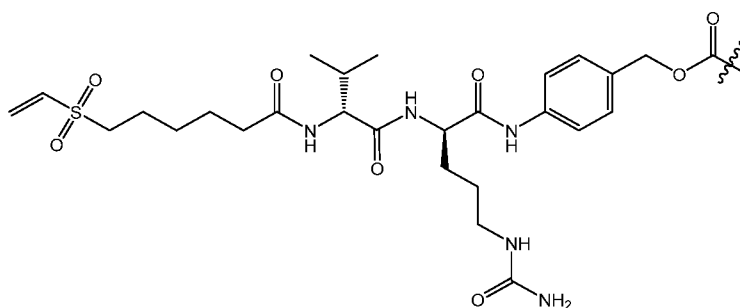
(IVb.13)



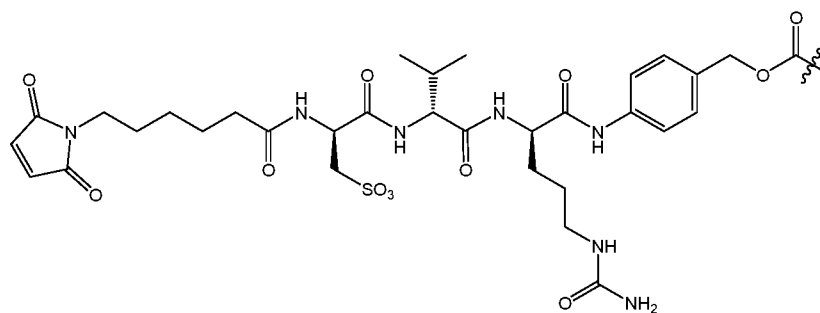
(IVb.14)



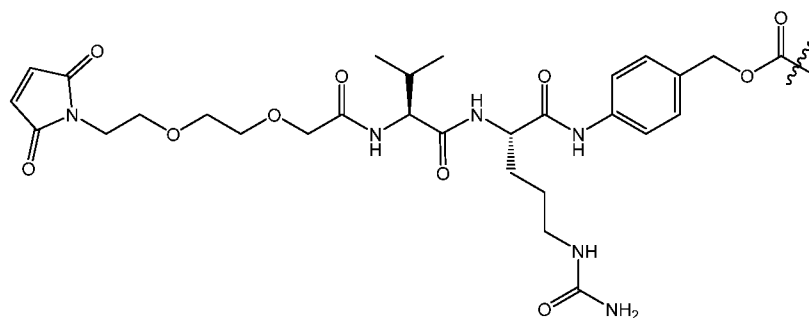
(IVb.15)



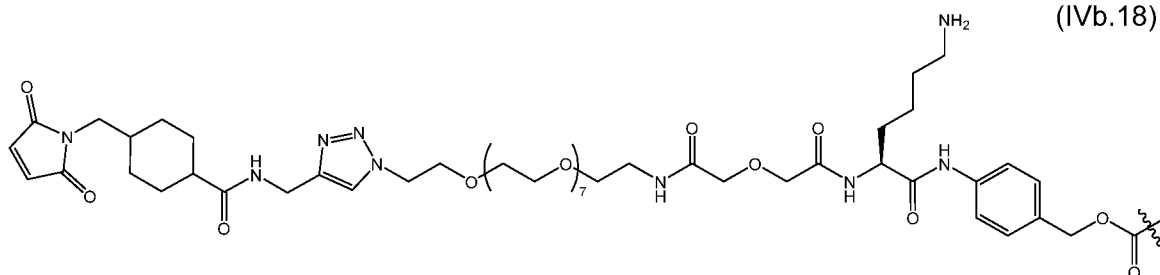
(IVb.16)



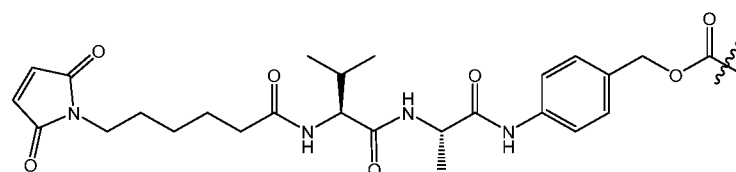
(IVb.17)



(IVb.18)

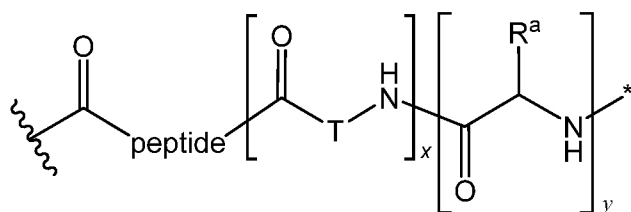


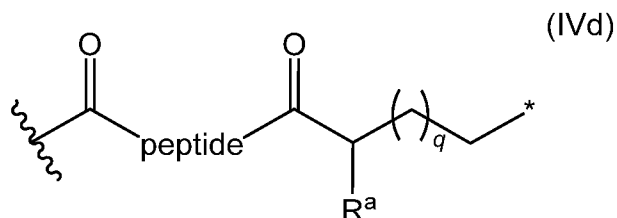
(IVb.19)



[0204] In certain embodiments, the linker comprises an enzymatically cleavable peptide moiety, for example, a linker comprising structural formula (IVc) or (IVd):

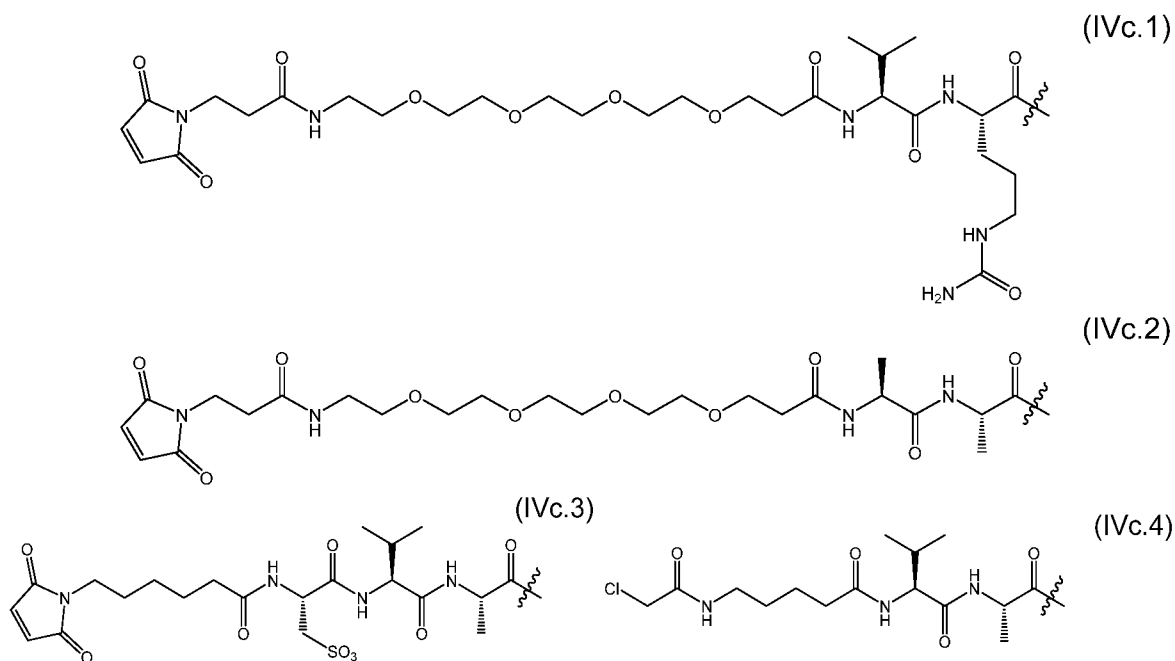
(IVc)

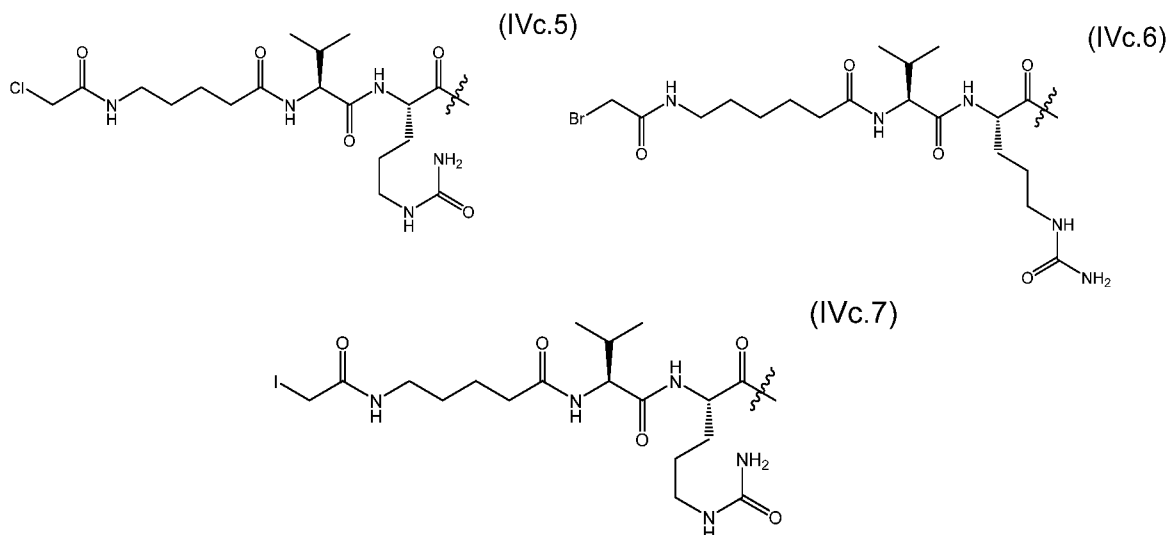




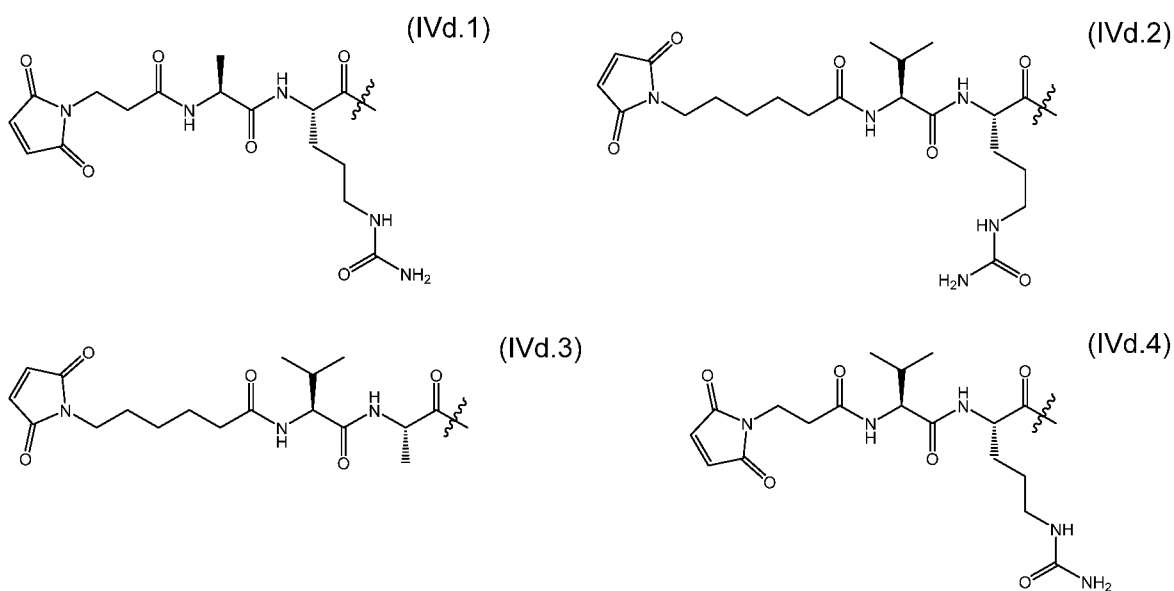
or a salt thereof, wherein: peptide represents a peptide (illustrated C→N and not showing the carboxy and amino “termini”) cleavable by a lysosomal enzyme; T represents a polymer comprising one or more ethylene glycol units or an alkylene chain, or combinations thereof; R^a is selected from hydrogen, alkyl, sulfonate and methyl sulfonate; p is an integer ranging from 0 to 5; q is 0 or 1; x is 0 or 1; y is 0 or 1; $\times$ represents the point of attachment of the linker to a cytotoxic and/or cytostatic agent; and * represents the point of attachment to the remainder of the linker.

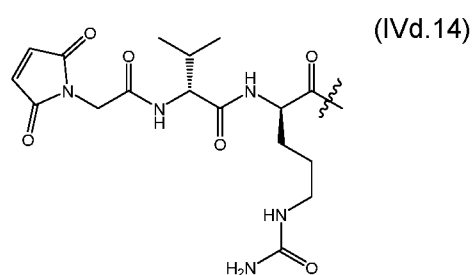
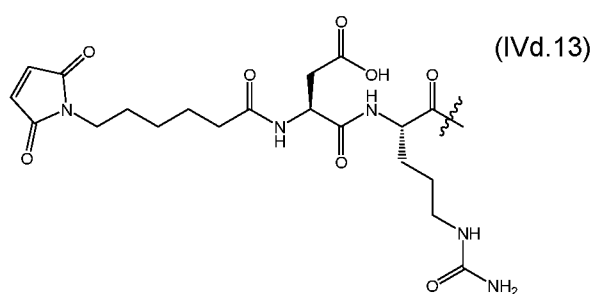
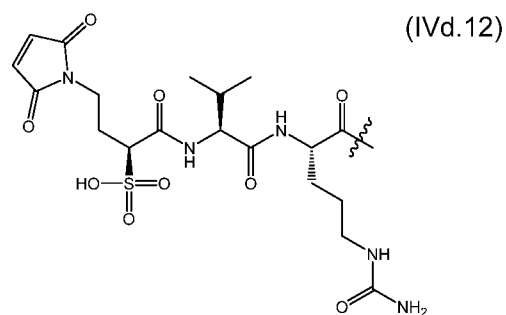
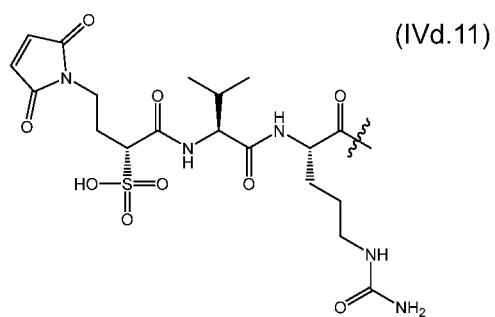
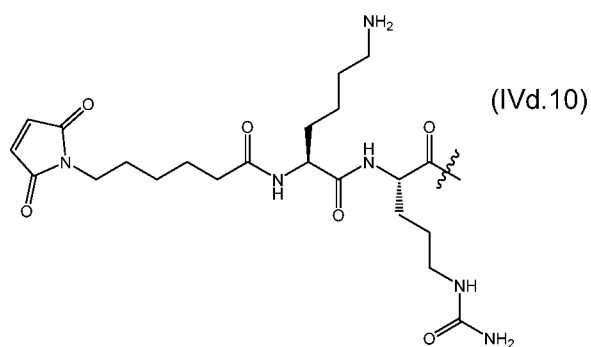
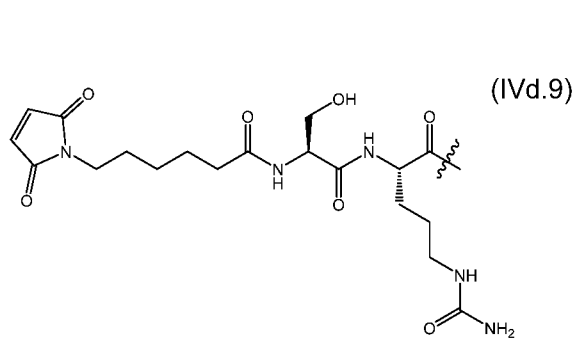
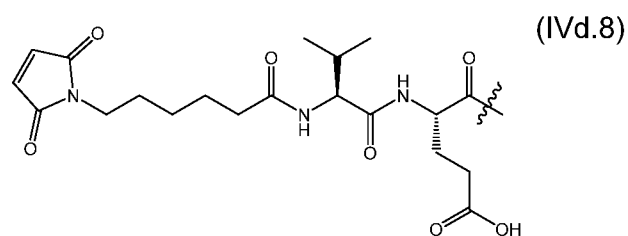
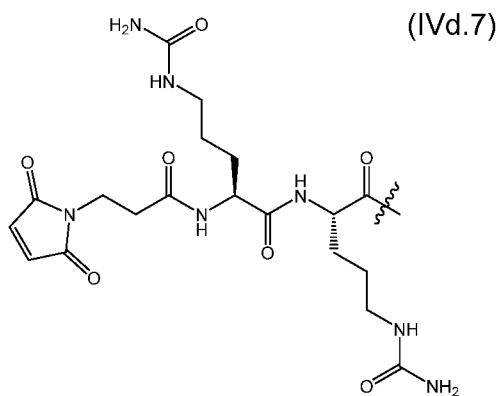
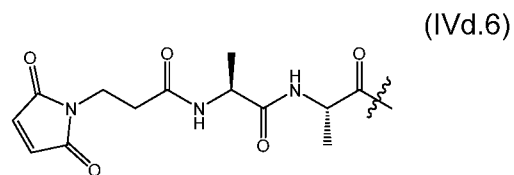
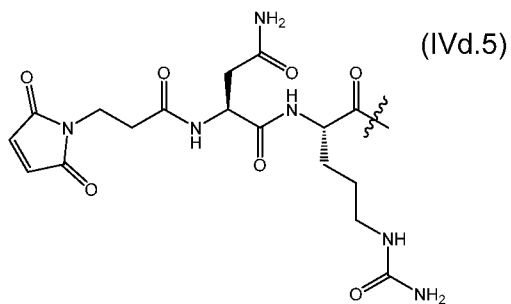
[0205] Specific exemplary embodiments of linkers according to structural formula (IVc) that may be included in the anti-glyco-LAMP1 ADCs of the disclosure include the linkers illustrated below (as illustrated, the linkers include a group suitable for covalently linking the linker to an antibody):

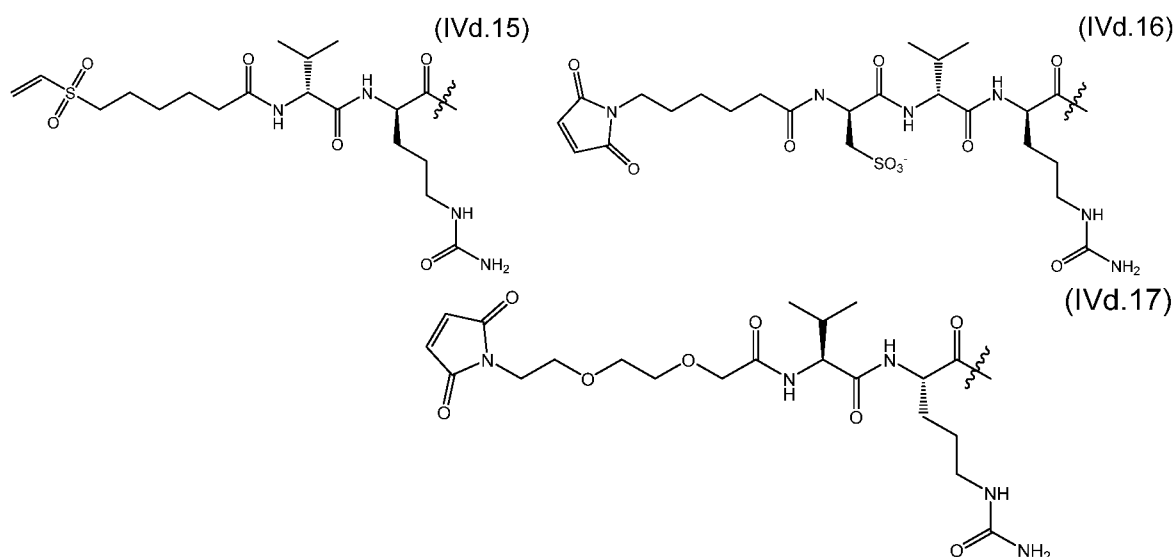




[0206] Specific exemplary embodiments of linkers according to structural formula (IVd) that may be included in the anti-glyco-LAMP1 ADCs of the disclosure include the linkers illustrated below (as illustrated, the linkers include a group suitable for covalently linking the linker to an antibody):







[0207] In certain embodiments, the linker comprising structural formula (IVa), (IVb), (IVc), or (IVd) further comprises a carbonate moiety cleavable by exposure to an acidic medium. In particular embodiments, the linker is attached through an oxygen to a cytotoxic and/or cytostatic agent.

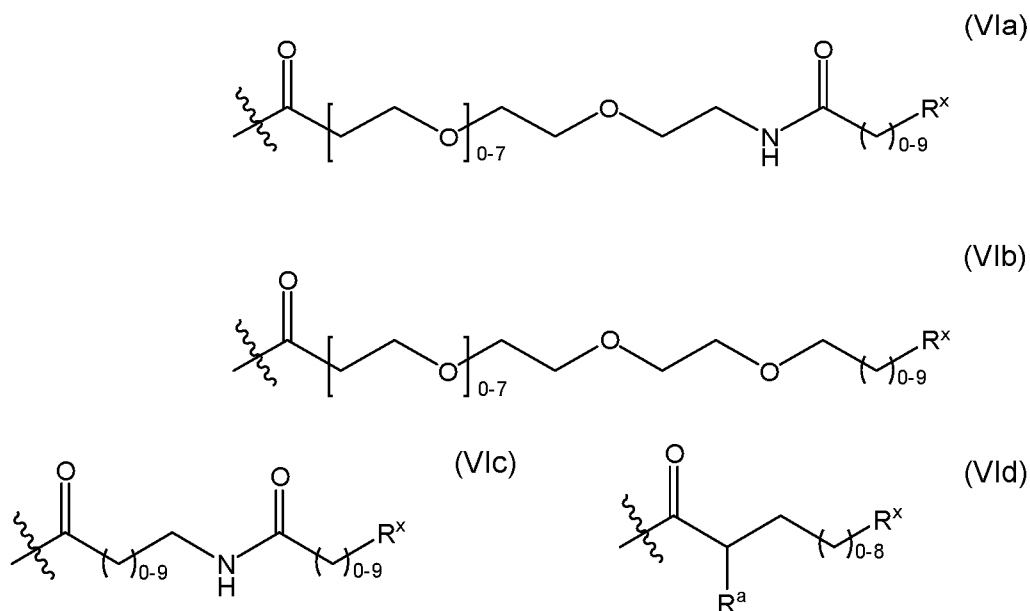
5.2.4. Non-Cleavable Linkers

[0208] Although cleavable linkers may provide certain advantages, the linkers comprising the anti-glyco-LAMP1 ADC of the disclosure need not be cleavable. For noncleavable linkers, the release of drug does not depend on the differential properties between the plasma and some cytoplasmic compartments. The release of the drug is postulated to occur after internalization of the ADC via antigen-mediated endocytosis and delivery to lysosomal compartment, where the antibody is degraded to the level of amino acids through intracellular proteolytic degradation. This process releases a drug derivative, which is formed by the drug, the linker, and the amino acid residue to which the linker was covalently attached. The amino acid drug metabolites from conjugates with noncleavable linkers are more hydrophilic and generally less membrane permeable, which leads to less bystander effects and less nonspecific toxicities compared to conjugates with a cleavable linker. In general, ADCs with noncleavable linkers have greater stability in circulation than ADCs with cleavable linkers. Non-cleavable linkers may be alkylene chains, or maybe polymeric in nature, such as, for example, based upon polyalkylene glycol polymers, amide polymers, or may include segments of alkylene chains, polyalkylene glycols and/or amide polymers.

[0209] A variety of non-cleavable linkers used to link drugs to antibodies have been described. See, Jeffrey *et al.*, 2006, *Bioconjug. Chem.* 17; 831-840; Jeffrey *et al.*, 2007, *Bioorg. Med. Chem. Lett.* 17:2278-2280; and Jiang *et al.*, 2005, *J. Am. Chem. Soc.* 127:11254-11255, each

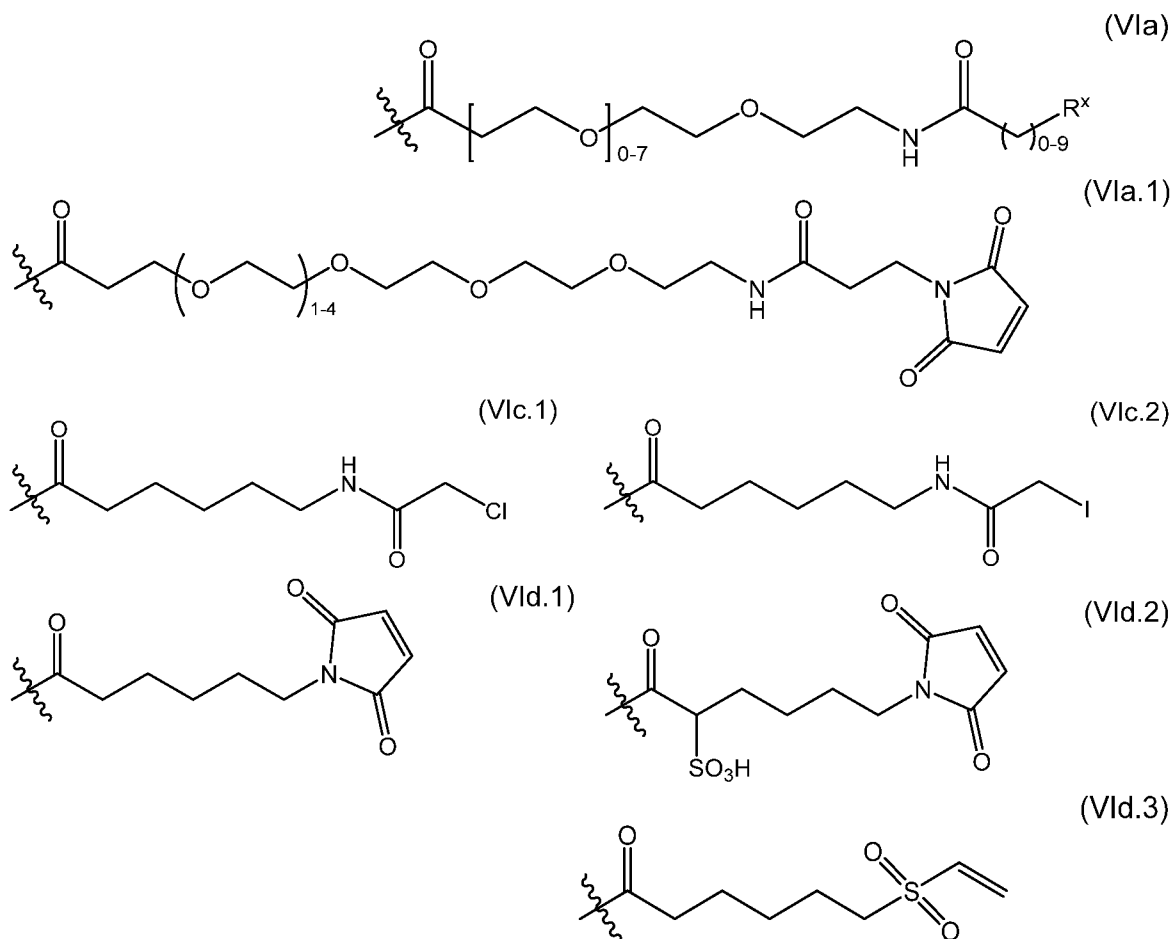
of which is incorporated herein by reference. All of these linkers may be included in the anti-glyco-LAMP1 ADCs of the disclosure.

[0210] In certain embodiments, the linker is non-cleavable *in vivo*, for example a linker according to structural formula (VIa), (VIb), (VIc) or (VIId) (as illustrated, the linkers include a group suitable for covalently linking the linker to an antibody:



or salts thereof, wherein: R^a is selected from hydrogen, alkyl, sulfonate and methyl sulfonate; R^x is a moiety including a functional group capable of covalently linking the linker to an antibody; and represents the point of attachment of the linker to a cytotoxic and/or cytostatic agent.

[0211] Specific exemplary embodiments of linkers according to structural formula (VIa)-(VIId) that may be included in the anti-glyco-LAMP1 ADCs of the disclosure include the linkers illustrated below (as illustrated, the linkers include a group suitable for covalently linking the linker to an antibody, and represents the point of attachment to a cytotoxic and/or cytostatic agent):

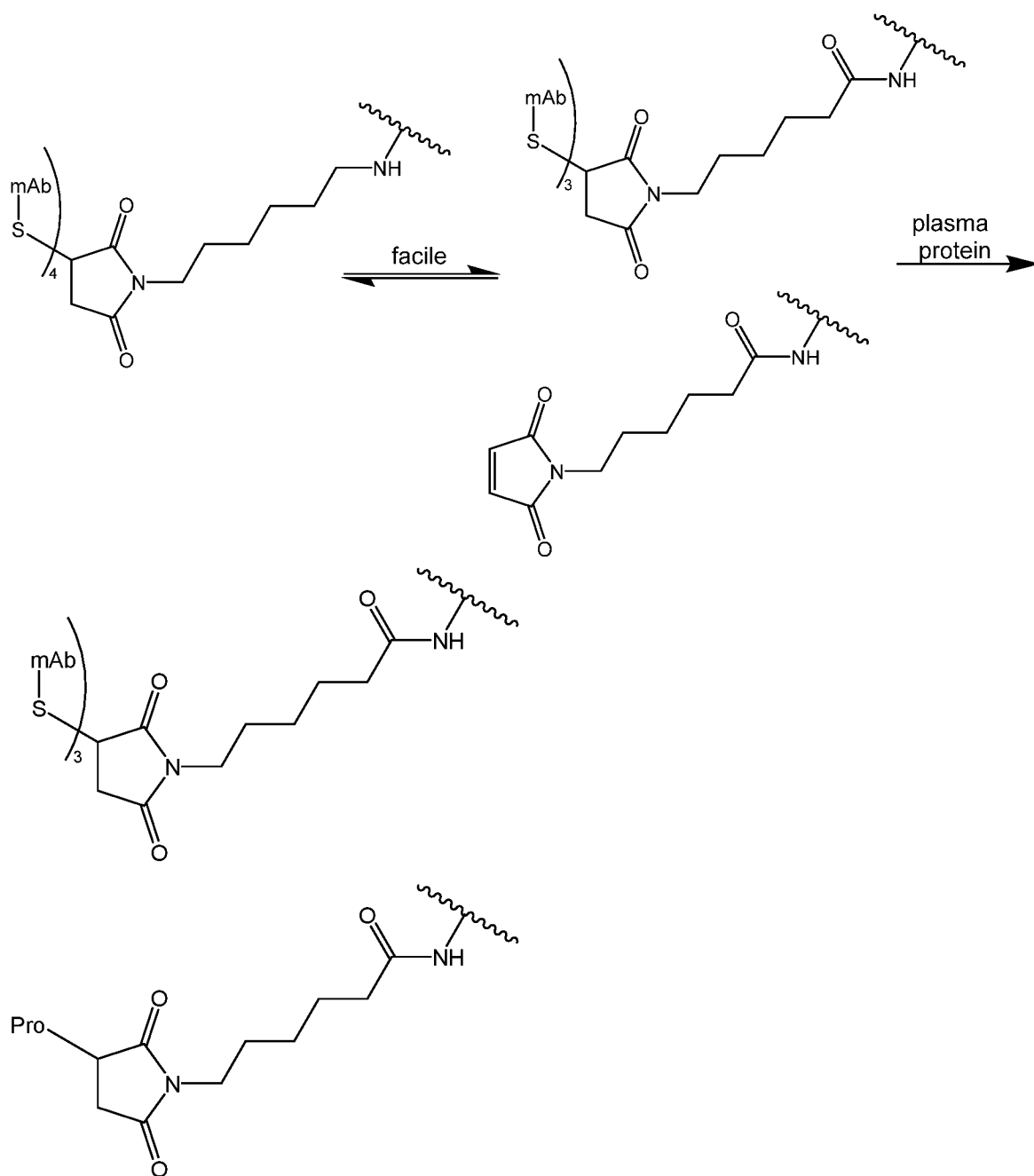


5.2.5. Groups Used to Attach Linkers to Antibodies

[0212] A variety of groups may be used to attach linker-drug synthons to antibodies to yield ADCs. Attachment groups can be electrophilic in nature and include: maleimide groups, activated disulfides, active esters such as NHS esters and HOBt esters, haloformates, acid halides, alkyl and benzyl halides such as haloacetamides. As discussed below, there are also emerging technologies related to "self-stabilizing" maleimides and "bridging disulfides" that can be used in accordance with the disclosure. The specific group used will depend, in part, on the site of attachment to the antibody.

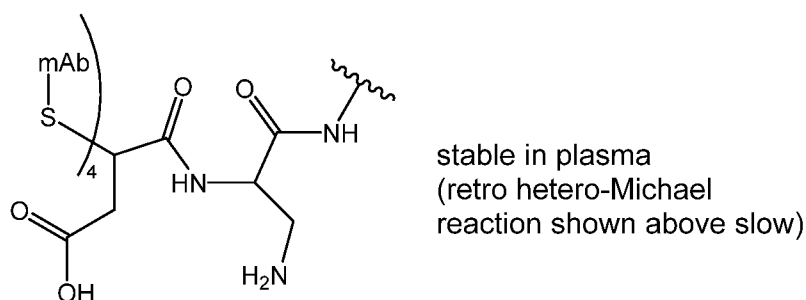
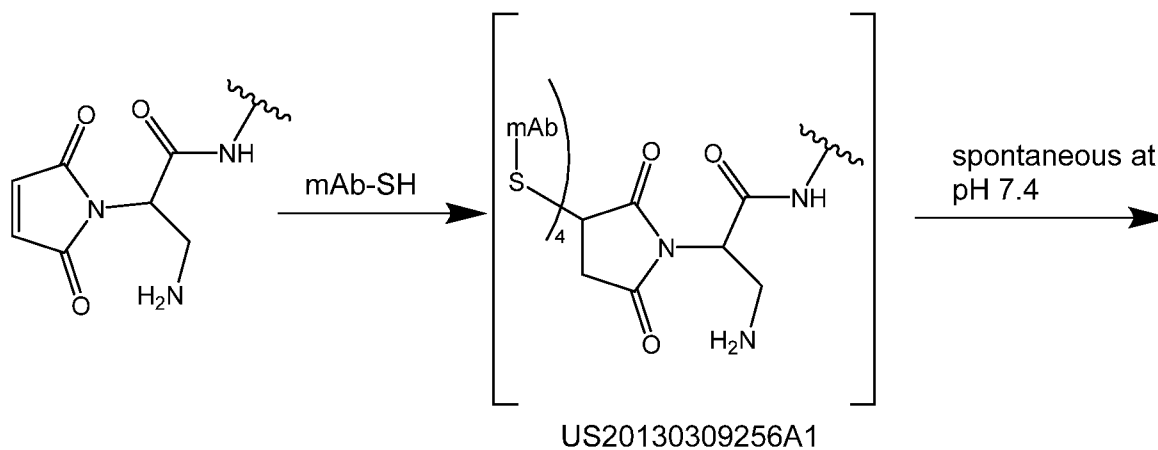
[0213] One example of a "self-stabilizing" maleimide group that hydrolyzes spontaneously under antibody conjugation conditions to give an ADC species with improved stability is depicted in the schematic below. See US20130309256 A1; also Lyon *et al.*, Nature Biotech published online, doi:10.1038/nbt.2968.

Normal system:

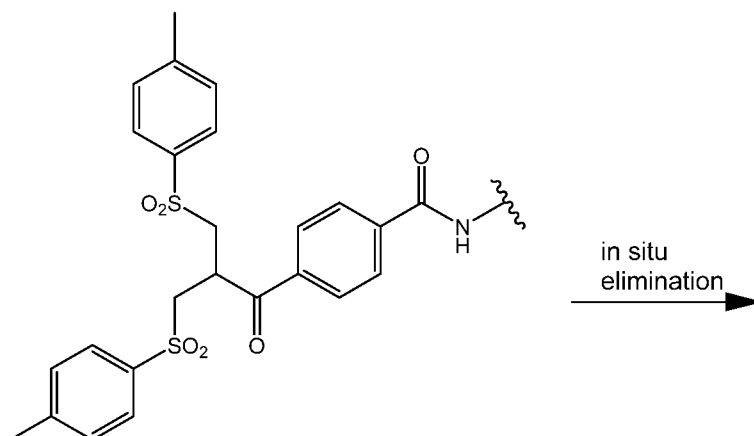


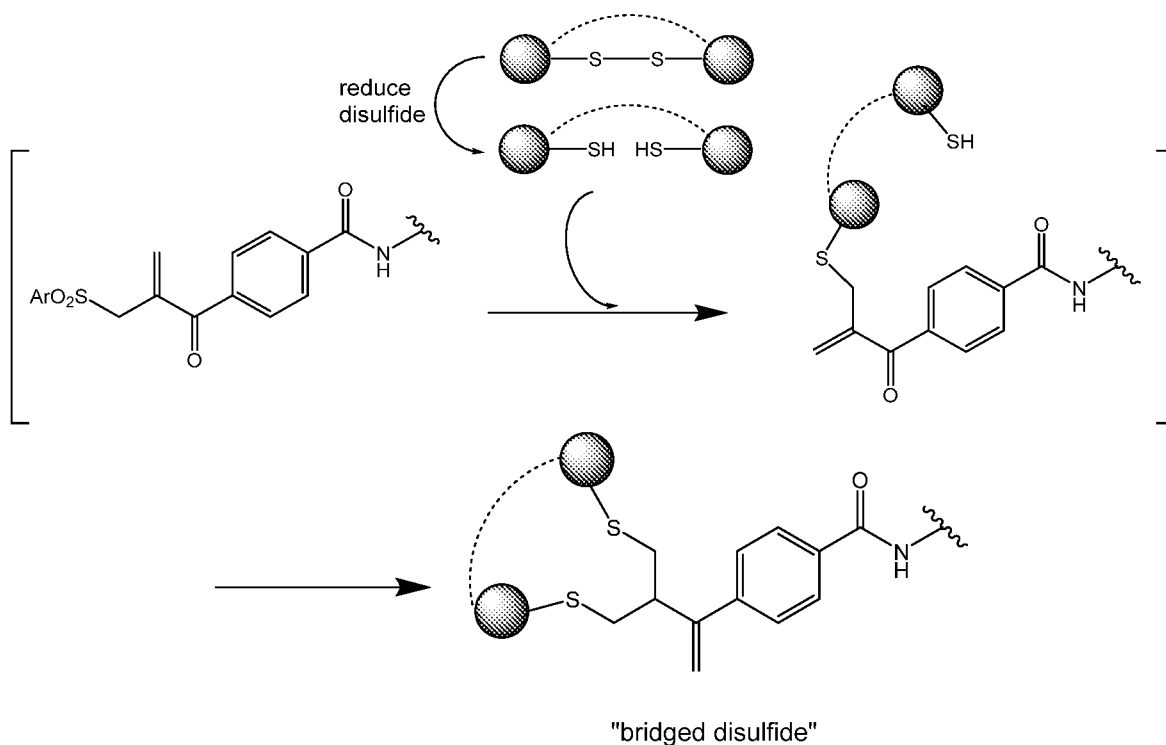
Leads to "DAR loss" over time

SGN MaIDPR (maleimido dipropylamino) system:

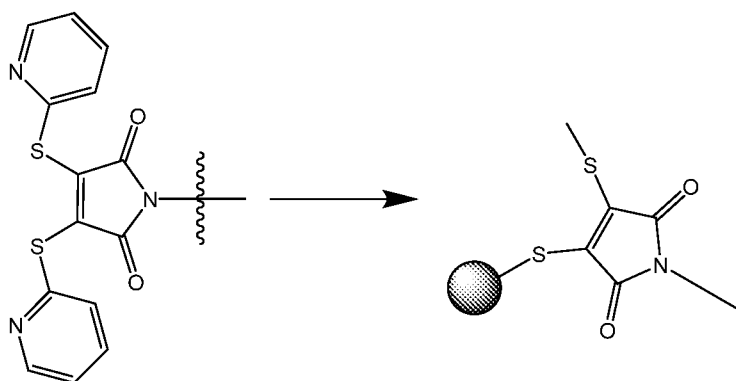


[0214] Polytherics has disclosed a method for bridging a pair of sulfhydryl groups derived from reduction of a native hinge disulfide bond. See, Badescu *et al.*, 2014, Bioconjugate Chem. 25:1124-1136. The reaction is depicted in the schematic below. An advantage of this methodology is the ability to synthesize enriched DAR4 ADCs by full reduction of IgGs (to give 4 pairs of sulfhydryls) followed by reaction with 4 equivalents of the alkylating agent. ADCs containing "bridged disulfides" are also claimed to have increased stability.





[0215] Similarly, as depicted below, a maleimide derivative (1, below) that is capable of bridging a pair of sulfhydryl groups has been developed. See WO2013/085925.



5.2.6. Linker Selection Considerations

[0216] As is known by skilled artisans, the linker selected for a particular ADC may be influenced by a variety of factors, including but not limited to, the site of attachment to the antibody (e.g., lys, cys or other amino acid residues), structural constraints of the drug pharmacophore and the lipophilicity of the drug. The specific linker selected for an ADC should seek to balance these different factors for the specific antibody/drug combination. For a review of the factors that are influenced by choice of linkers in ADCs, see Nolting, Chapter 5 "Linker Technology in Antibody-Drug Conjugates," In: Antibody-Drug Conjugates: Methods in Molecular

Biology, vol. 1045, pp. 71-100, Laurent Ducry (Ed.), Springer Science & Business Media, LLC, 2013.

[0217] For example, ADCs have been observed to effect killing of bystander antigen-negative cells present in the vicinity of the antigen-positive tumor cells. The mechanism of bystander cell killing by ADCs has indicated that metabolic products formed during intracellular processing of the ADCs may play a role. Neutral cytotoxic metabolites generated by metabolism of the ADCs in antigen-positive cells appear to play a role in bystander cell killing while charged metabolites may be prevented from diffusing across the membrane into the medium and therefore cannot affect bystander killing. In certain embodiments, the linker is selected to attenuate the bystander killing effect caused by cellular metabolites of the ADC. In certain embodiments, the linker is selected to increase the bystander killing effect.

[0218] The properties of the linker may also impact aggregation of the ADC under conditions of use and/or storage. Typically, ADCs reported in the literature contain no more than 3-4 drug molecules per antibody molecule (see, e.g., Chari, 2008, *Acc Chem Res* 41:98-107). Attempts to obtain higher drug-to-antibody ratios ("DAR") often failed, particularly if both the drug and the linker were hydrophobic, due to aggregation of the ADC (King *et al.*, 2002, *J Med Chem* 45:4336-4343; Hollander *et al.*, 2008, *Bioconjugate Chem* 19:358-361; Burke *et al.*, 2009 *Bioconjugate Chem* 20:1242-1250). In many instances, DARs higher than 3-4 could be beneficial as a means of increasing potency. In instances where the cytotoxic and/or cytostatic agent is hydrophobic in nature, it may be desirable to select linkers that are relatively hydrophilic as a means of reducing ADC aggregation, especially in instances where DARs greater than 3-4 are desired. Thus, in certain embodiments, the linker incorporates chemical moieties that reduce aggregation of the ADCs during storage and/or use. A linker may incorporate polar or hydrophilic groups such as charged groups or groups that become charged under physiological pH to reduce the aggregation of the ADCs. For example, a linker may incorporate charged groups such as salts or groups that deprotonate, e.g., carboxylates, or protonate, e.g., amines, at physiological pH.

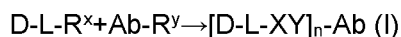
[0219] Exemplary polyvalent linkers that have been reported to yield DARs as high as 20 that may be used to link numerous cytotoxic and/or cytostatic agents to an antibody are described in WO 2009/073445; WO 2010/068795; WO 2010/138719; WO 2011/120053; WO 2011/171020; WO 2013/096901; WO 2014/008375; WO 2014/093379; WO 2014/093394; WO 2014/093640, the content of which are incorporated herein by reference in their entireties.

[0220] In particular embodiments, the aggregation of the ADCs during storage or use is less than about 10% as determined by size-exclusion chromatography (SEC). In particular embodiments, the aggregation of the ADCs during storage or use is less than 10%, such as less than about 5%, less than about 4%, less than about 3%, less than about 2%, less than

about 1%, less than about 0.5%, less than about 0.1%, or even lower, as determined by size-exclusion chromatography (SEC).

5.2.7. Methods of Making Anti-Glyco-LAMP1 ADCs

[0221] The anti-glyco-LAMP1 ADCs of the disclosure may be synthesized using chemistries that are well-known. The chemistries selected will depend upon, among other things, the identity of the cytotoxic and/or cytostatic agent(s), the linker and the groups used to attach linker to the antibody. Generally, ADCs according to formula (I) may be prepared according to the following scheme:



[0222] where D, L, Ab, XY and n are as previously defined, and R^x and R^y represent complementary groups capable of forming a covalent linkages with one another, as discussed above.

[0223] The identities of groups R^x and R^y will depend upon the chemistry used to link synthon D-L- R^x to the antibody. Generally, the chemistry used should not alter the integrity of the antibody, for example its ability to bind its target. Preferably, the binding properties of the conjugated antibody will closely resemble those of the unconjugated antibody. A variety of chemistries and crosstechniques for conjugating molecules to biological molecules such as antibodies are known in the art and in particular to antibodies, are well-known. See, e.g., Amon *et al.*, "Monoclonal Antibodies For Immunotargeting Of Drugs In Cancer Therapy," in: Monoclonal Antibodies And Cancer Therapy, Reisfeld *et al.* Eds., Alan R. Liss, Inc., 1985; Hellstrom *et al.*, "Antibodies For Drug Delivery," in: Controlled Drug Delivery, Robinson *et al.* Eds., Marcel Dekker, Inc., 2nd Ed. 1987; Thorpe, "Antibody Carriers Of Cytotoxic Agents In Cancer Therapy: A Review," in: Monoclonal Antibodies '84: Biological And Clinical Applications, Pinchera *et al.*, Eds., 1985; "Analysis, Results, and Future Prospective of the Therapeutic Use of Radiolabeled Antibody In Cancer Therapy," in: Monoclonal Antibodies For Cancer Detection And Therapy, Baldwin *et al.*, Eds., Academic Press, 1985; Thorpe *et al.*, 1982, Immunol. Rev. 62:119-58; PCT publication WO 89/12624. Any of these chemistries may be used to link the synthons to an antibody.

[0224] A number of functional groups R^x and chemistries useful for linking synthons to accessible lysine residues are known and include, by way of example and not limitation, NHS-esters and isothiocyanates.

[0225] A number of functional groups R^x and chemistries useful for linking synthons to accessible free sulfhydryl groups of cysteine residues are known and include, by way of example and not limitation haloacetyls and maleimides.

[0226] However, conjugation chemistries are not limited to available side chain groups. Side chains such as amines may be converted to other useful groups, such as hydroxyls, by linking

an appropriate small molecule to the amine. This strategy can be used to increase the number of available linking sites on the antibody by conjugating multifunctional small molecules to side chains of accessible amino acid residues of the antibody. Functional groups R^x suitable for covalently linking the synthons to these "converted" functional groups are then included in the synthons.

[0227] The antibody may also be engineered to include amino acid residues for conjugation. An approach for engineering antibodies to include non-genetically encoded amino acid residues useful for conjugating drugs in the context of ADCs is described by Axup *et al.*, 2012, Proc Natl Acad Sci USA. 109(40):16101-16106, as are chemistries and functional group useful for linking synthons to the non-encoded amino acids.

[0228] Typically, the synthons are linked to the side chains of amino acid residues of the antibody, including, for example, the primary amino group of accessible lysine residues or the sulfhydryl group of accessible cysteine residues. Free sulfhydryl groups may be obtained by reducing interchain disulfide bonds.

[0229] For linkages where R^y is a sulfhydryl group (for example, when R^x is a maleimide), the antibody is generally first fully or partially reduced to disrupt interchain disulfide bridges between cysteine residues.

[0230] Cysteine residues that do not participate in disulfide bridges may be engineered into an antibody by mutation of one or more codons. Reducing these unpaired cysteines yields a sulfhydryl group suitable for conjugation. Preferred positions for incorporating engineered cysteines include, by way of example and not limitation, positions S112C, S113C, A114C, S115C, A176C, 5180C, S252C, V286C, V292C, S357C, A359C, S398C, S428C (Kabat numbering) on the human IgG₁ heavy chain and positions V110C, S114C, S121C, S127C, S168C, V205C (Kabat numbering) on the human Ig kappa light chain (see, e.g., U.S. Pat. No. 7,521,541, U.S. Pat. No. 7,855,275 and U.S. Pat. No. 8,455,622).

[0231] As will be appreciated by skilled artisans, the number of cytotoxic and/or cytostatic agents linked to an antibody molecule may vary, such that a collection of ADCs may be heterogeneous in nature, where some antibodies contain one linked agent, some two, some three, *etc.* (and some none). The degree of heterogeneity will depend upon, among other things, the chemistries used for linking the cytotoxic and/or cytostatic agents. For example, where the antibodies are reduced to yield sulfhydryl groups for attachment, heterogeneous mixtures of antibodies having zero, 2, 4, 6 or 8 linked agents per molecule are often produced. Furthermore, by limiting the molar ratio of attachment compound, antibodies having zero, 1, 2, 3, 4, 5, 6, 7 or 8 linked agents per molecule are often produced. Thus, it will be understood that depending upon context, stated DARs may be averages for a collection of antibodies. For example, "DAR4" can refer to an ADC preparation that has not been subjected to purification to isolate specific DAR peaks and can comprise a heterogeneous mixture of ADC molecules

having different numbers of cytostatic and/or cytotoxic agents attached per antibody (e.g., 0, 2, 4, 6, 8 agents per antibody), but has an average drug-to-antibody ratio of 4. Similarly, in some embodiments, “DAR2” refers to a heterogeneous ADC preparation in which the average drug-to-antibody ratio is 2.

[0232] When enriched preparations are desired, antibodies having defined numbers of linked cytotoxic and/or cytostatic agents may be obtained via purification of heterogeneous mixtures, for example, via column chromatography, e.g., hydrophobic interaction chromatography.

[0233] Purity may be assessed by a variety of methods, as is known in the art. As a specific example, an ADC preparation may be analyzed via HPLC or other chromatography and the purity assessed by analyzing areas under the curves of the resultant peaks.

5.3 Chimeric Antigen Receptors

[0234] The present disclosure provides chimeric antigen receptors (CARs) comprising the anti-glyco-LAMP1 antibodies or antigen-binding fragments described herein. In some embodiments, the CAR comprises one or more scFvs (e.g., one or two) as described herein. For example, a CAR can comprise two scFvs covalently connected by a linker sequence (e.g., of 4-15 amino acids). Exemplary linkers include GGGGS (SEQ ID NO:159) and (GGGGS)₃ (SEQ ID NO:160).

[0235] The CARs of the disclosure typically comprise an extracellular domain operably linked to a transmembrane domain which is in turn operably linked to an intracellular domain for signaling. The CARs can further comprise a signal peptide at the N-terminus of the extracellular domain (e.g., a human CD8 signal peptide). In some embodiments, a CAR of the disclosure comprises a human CD8 signal peptide comprising the amino acid sequence MALPVTALLLPLALLLHAARP (SEQ ID NO:161).

[0236] The extracellular domains of the CARs of the disclosure comprise the sequence of an anti-glyco-LAMP1 antibody or antigen-binding fragment (e.g., as described in Section 5.1 or numbered embodiments 558 to 591).

[0237] Exemplary transmembrane domain sequence and intracellular domain sequences are described in Section 5.3.1 and 5.3.2, respectively.

[0238] Several fusion proteins described herein (e.g., numbered embodiments 558 to 591) are CARs, and the CAR-related disclosures apply to such fusion proteins. Other fusion proteins described herein (e.g., in numbered embodiments 602 to 695) are chimeric T cell receptors (TCRs), and the chimeric TCR-related disclosures apply to such fusion proteins.

5.3.1. Transmembrane Domain

[0239] With respect to the transmembrane domain, the CAR can be designed to comprise a transmembrane domain that is operably linked (e.g., fused) to the extracellular domain of the CAR.

[0240] The transmembrane domain may be derived either from a natural or from a synthetic source. Where the source is natural, the domain may be derived from any membrane-bound or transmembrane protein. Transmembrane regions of particular use in this disclosure may be derived from (*i.e.*, comprise at least the transmembrane region(s) of) the alpha, beta or zeta chain of the T-cell receptor, CD28, CD3 epsilon, CD45, CD4, CD5, CD8, CD9, CD16, CD22, CD33, CD37, CD64, CD80, CD86, CD134, CD137, CD154. In some instances, a variety of human hinges can be employed as well including the human Ig (immunoglobulin) hinge.

[0241] In one embodiment, the transmembrane domain is synthetic (*i.e.*, non-naturally occurring). Examples of synthetic transmembrane domains are peptides comprising predominantly hydrophobic residues such as leucine and valine. Preferably a triplet of phenylalanine, tryptophan and valine will be found at each end of a synthetic transmembrane domain. Optionally, a short oligo- or polypeptide linker, preferably between 2 and 10 amino acids in length may form the linkage between the transmembrane domain and the cytoplasmic signaling domain of the CAR. A glycine-serine doublet provides a particularly suitable linker.

[0242] In one embodiment, the transmembrane domain in the CAR of the disclosure is the CD8 transmembrane domain. In one embodiment, the CD8 transmembrane domain comprises the amino acid sequence YLHLGALGRDLWGSPVTGYHPLL (SEQ ID NO:162).

[0243] In one embodiment, the transmembrane domain in the CAR of the disclosure is the CD28 transmembrane domain. In one embodiment, the CD28 transmembrane domain comprises the amino acid sequence FWVLVVGGVLACYSLLVTVAFIIFWW (SEQ ID NO:163).

[0244] In some instances, the transmembrane domain of the CAR of the disclosure is linked to the extracellular domain by a CD8a hinge domain. In one embodiment, the CD8a hinge domain comprises the amino acid sequence

TTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFAC (SEQ ID NO:164). In another

embodiment, the CD8a hinge domain comprises the amino acid sequence

TTTPAPRPPTPAPTIASPLSLRPEACRPAAGGAVHTRGLDFACD (SEQ ID NO:165). In another

embodiment, the CD8a hinge domain comprises the amino acid sequence

TTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACD (SEQ ID NO:220).

[0245] In some instances, the transmembrane domain of the CAR of the disclosure is linked to the extracellular domain by a human IgG4-short hinge. In one embodiment, the human IgG4-short hinge comprises the amino acid sequence ESKYGPPCPSCP (SEQ ID NO:166).

[0246] In some instances, the transmembrane domain of the CAR of the disclosure is linked to the extracellular domain by a human IgG4-long hinge. In one embodiment, the human IgG4-long hinge comprises the amino acid sequence

ESKYGPPCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDG
VEVHNAKTKPREEQFQSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPR

EPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPVLDSGDSFFLY
SRLTVDKSRWQEGNVFSCSVMHEALHNHYTQKSLSLGLGKM (SEQ ID NO:167).

5.3.2. Intracellular Domain

[0247] The intracellular signaling domain of the CAR of the disclosure is responsible for activation of at least one of the normal effector functions of the immune cell in which the CAR is expressed. The term “effector function” refers to a specialized function of a cell. Effector function of a T cell, for example, may be cytolytic activity or helper activity including the secretion of cytokines. Thus the term “intracellular signaling domain” refers to the portion of a protein which transduces the effector function signal and directs the cell to perform a specialized function. While usually the entire intracellular signaling domain can be employed, in many cases it is not necessary to use the entire chain. To the extent that a truncated portion of the intracellular signaling domain is used, such truncated portion may be used in place of the intact chain as long as it transduces the effector function signal. The term intracellular signaling domain is thus meant to include any truncated portion of the intracellular signaling domain sufficient to transduce the effector function signal.

[0248] Preferred examples of intracellular signaling domains for use in the CAR of the disclosure include the cytoplasmic sequences of the T cell receptor (TCR) and co-receptors that act in concert to initiate signal transduction following antigen receptor engagement, as well as any derivative or variant of these sequences and any synthetic sequence that has the same functional capability.

[0249] Signals generated through the TCR alone may be insufficient for full activation of the T cell and a secondary or co-stimulatory signal is also required. Thus, T cell activation can be said to be mediated by two distinct classes of cytoplasmic signaling sequence: those that initiate antigen-dependent primary activation through the TCR (primary cytoplasmic signaling sequences) and those that act in an antigen-independent manner to provide a secondary or co-stimulatory signal (secondary cytoplasmic signaling sequences).

[0250] Primary cytoplasmic signaling sequences regulate primary activation of the TCR complex either in a stimulatory way, or in an inhibitory way. Primary cytoplasmic signaling sequences that act in a stimulatory manner may contain signaling motifs which are known as immunoreceptor tyrosine-based activation motifs or ITAMs.

[0251] Examples of ITAM containing primary cytoplasmic signaling sequences that are of particular use in the CARs of the disclosure include those derived from TCR zeta, FcR gamma, FcR beta, CD3 gamma, CD3 delta, CD3 epsilon, CD5, CD22, CD79a, CD79b, and CD66d. It is particularly preferred that cytoplasmic signaling molecule in the CAR of the disclosure comprises a cytoplasmic signaling sequence from CD3-zeta.

[0252] In a preferred embodiment, the cytoplasmic domain of the CAR is designed to include an ITAM containing primary cytoplasmic signaling sequences domain (e.g., that of CD3-zeta) by itself or combined with any other desired cytoplasmic domain(s) useful in the context of the CAR of the disclosure. For example, the cytoplasmic domain of the CAR can include a CD3 zeta chain portion and a costimulatory signaling region.

[0253] The costimulatory signaling region refers to a portion of the CAR comprising the intracellular domain of a costimulatory molecule. A costimulatory molecule is a cell surface molecule other than an antigen receptor or its ligands that is required for an efficient response of lymphocytes to an antigen. Examples of such molecules include CD27, CD28, 4-1BB (CD137), OX40, CD30, CD40, PD-1, ICOS, lymphocyte function-associated antigen-1 (LFA-1), CD2, CD7, LIGHT, NKG2C, B7-H3, and a ligand that specifically binds with CD83, DAP10, GITR, and the like.

[0254] The cytoplasmic signaling sequences within the cytoplasmic signaling portion of the CAR of the disclosure may be linked to each other in a random or specified order. Optionally, a short oligo- or polypeptide linker, preferably between 2 and 10 amino acids in length may form the linkage. A glycine-serine doublet provides a particularly suitable linker.

[0255] In one embodiment, the cytoplasmic domain comprises the signaling domain of CD3-zeta and the signaling domain of CD28. In some embodiments, the signaling domain of CD3-zeta comprises the amino acid sequence
RVKFSSADAPAYQQGQNQLYNELNLGRREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYN
ELQKDKMAEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQALPPR (SEQ ID
NO:168). In some embodiments, the signaling domain of CD28 comprises the amino acid sequence RSKRSRLHSDYMNMTPRRPGPTRKHYQPYAPPRDFAAYRS (SEQ ID NO:169).

[0256] In another embodiment, the cytoplasmic domain comprises the signaling domain of CD3-zeta and the signaling domain of 4-1BB.

[0257] In another embodiment, the cytoplasmic domain comprises the signaling domain of CD3-zeta and the signaling domain of CD2. In some embodiments, the signaling domain of CD2 comprises the amino acid sequence
TKRKKQRSRRNDEELETRAHRVATEERGRKPHQIPASTPQNPA TSQHPPPPGHRSQAPSHR
PPPPGHRVQHQPQKRPPAPSGTQVHQKGPPLPRPRVQPKPPHGA AENSLSPSSN (SEQ ID
NO:170).

[0258] In another embodiment, the cytoplasmic domain comprises the signaling domain of CD3-zeta, the signaling domain of CD28, and the signaling domain of CD2.

[0259] In another embodiment, the cytoplasmic domain comprises the signaling domain of CD3-zeta, the signaling domain of 4-1BB, and the signaling domain of CD2.

[0260] Inclusion of the CD2 signaling domain in the cytoplasmic domain allows for the tuning of CAR T cell cytokine production (see US Pat. No. 9,783,591, the contents of which are incorporated herein by reference in their entireties). As disclosed in US Pat. No. 9,783,591, inclusion of the CD2 signaling domain in the CAR cytoplasmic domain significantly alters CAR T cell cytokine production in both positive and negative directions, with the effect being dependent on the presence and identity of other costimulatory molecules in the costimulatory signaling region of the cytoplasmic domain. For example, in some embodiments, inclusion of the CD2 signaling domain and the CD28 signaling domain in the costimulatory signaling region of the cytoplasmic domain results in the release of significantly less IL2 relative to T cells expressing a CAR with CD28 but not CD2. A CAR T cell releasing less IL2 can result in reduced proliferation of immunosuppressive Treg cells. In some embodiments, inclusion of the CD2 signaling domain in the costimulatory signaling region of the cytoplasmic domain significantly reduces calcium influx in the CAR T cell. This has been shown to reduce activation-induced CAR T cell death.

5.4 Chimeric T Cell Receptors

[0261] The present disclosure provides chimeric T cell receptors (TCRs) comprising the anti-glyco-LAMP1 antibodies or antigen-binding fragments described herein. The chimeric TCRs provide an anti-glyco-LAMP1 specific antibody and TCR chimera that specifically binds to anti-glyco-LAMP1, and are capable of recruiting at least one TCR-associated signaling molecule (e.g., CD3 $\gamma\epsilon$, CD3 $\delta\epsilon$, and $\zeta\eta$). In some embodiments, the chimeric TCR comprises one or more antigen-binding fragments capable of binding glyco-LAMP1. Examples of antigen-binding fragments include by way of example and not limitation, Fab, Fab', F(ab')₂, Fv fragments, single chain Fv fragments (scFV) and single domain fragments. In some embodiments, an antigen-binding fragment of a chimeric T cell receptor comprises at least one anti-glyco-LAMP1 variable heavy chain and at least one anti-glyco-LAMP1 variable light chain as described herein.

[0262] TCRs occur as either an $\alpha\beta$ heterodimer or as a $\gamma\delta$ heterodimer, with T cells expressing either the $\alpha\beta$ form or the $\gamma\delta$ form TCR on the cell surface. The four chains (α , β , γ , δ) each have a characteristic extracellular structure consisting of a highly polymorphic "immunoglobulin variable region"-like N-terminal domain and an "immunoglobulin constant region"-like second domain. Each of these domains has a characteristic intra-domain disulfide bridge. The constant region is proximal to the cell membrane, followed by a connecting peptide, a transmembrane region and a short cytoplasmic tail. The covalent linkage between the 2 chains of the heterodimeric TCR is formed by the cysteine residue located within the short connecting peptide sequence bridging the extracellular constant domain and the transmembrane region which forms a disulfide bond with the paired TCR chain cysteine residue at the corresponding position (Lefranc and Lefranc, "The T Cell Receptor FactsBook," Academic Press, 2001).

[0263] Several examples of chimeric TCRs are known in the art. See, e.g., Kuwana *et al.*, Biochem Biophys Res Commun. 149(3):960-968; Gross *et al.*, 1989, Proc Natl Acad Sci USA. 86:10024-10028; Gross & Eshhar, 1992, FASEB J. 6(15):3370-3378; Liu *et al.*, 2021, Sci Transl Med, 13:eabb5191, WO 2016/187349, WO 2017/070608, WO 2020/029774, and US Patent No. 7,741,465, the contents of each of which are incorporated herein by reference in their entireties.

[0264] A chimeric TCR generally comprises a first polypeptide chain comprising a first TCR domain, a second polypeptide chain comprising a second TCR domain, and an anti-glyco-LAMP1 antigen binding fragment described herein. In some embodiments, the chimeric TCR comprises a single anti-glyco-LAMP1 antigen binding fragment. In other embodiments, the chimeric TCR comprises a two or more anti-glyco-LAMP1 antigen binding fragments. In certain embodiments, the chimeric TCR comprises two anti-glyco-LAMP1 antigen binding fragments.

[0265] In some embodiments, the anti-glyco-LAMP1 antigen binding fragment is an scFv described herein. In embodiments in which the chimeric TCR includes a single anti-glyco-LAMP1 antigen binding fragment, a single anti-glyco-LAMP1 scFv can be included in either the first polypeptide chain or the second polypeptide chain of the chimeric TCR. In embodiments in which the chimeric TCR includes, e.g., two anti-glyco-LAMP1 antigen binding fragments, two anti-glyco-LAMP1 scFVs can be included in either the first polypeptide chain or the second polypeptide chain of the chimeric TCR, or a first scFv can be included in the first polypeptide chain and a second scFv can be included in the second polypeptide chain. In embodiments in which two scFvs are included in one of either the first polypeptide chain or the second polypeptide chain of the chimeric TCR, the two scFvs can be linked via a peptide linker. In some embodiments, the chimeric TCR comprises two or more anti-glyco-LAMP1 scFvs having the same amino acid sequence. In other embodiments, the chimeric TCR comprises two or more anti-glyco-LAMP1 scFvs having different amino acid sequences.

[0266] In other embodiments, the anti-glyco-LAMP1 antigen binding fragment is an Fv fragment. In some embodiments, an anti-glyco-LAMP1 variable heavy chain (VH) described herein is included in one of the two polypeptide chains that associate to form the chimeric TCR. An anti-glyco-LAMP1 variable light chain (VL) described herein can be included in the polypeptide chain that does not include the anti-glyco-LAMP1 VH. When the first and second polypeptide chains dimerize, the anti-glyco-LAMP1 VH and VL are brought together to form an anti-glyco-LAMP1 Fv fragment. In some embodiments, the VH is included in the first polypeptide chain and the VL is included in the second polypeptide chain. In other embodiments, the VH is included in the second polypeptide chain and the VL is included in the first polypeptide chain.

[0267] In other embodiments, the anti-glyco-LAMP1 antigen fragment is a Fab- domain, comprising VH, VL, CH1, and CL domains. In some embodiments, an anti-glyco-LAMP1

variable heavy chain (VH) described herein and a CH1 domain is included in the first or second polypeptide chain. In some embodiments, an anti-glyco-LAMP1 variable light chain (VL) described herein and a CL domain are included in the first or second polypeptide chain that does not include the anti-glyco-LAMP1 VH and CH1. In other embodiments, an anti-glyco-LAMP1 variable heavy chain (VH) and a CL domain is included in the first or second polypeptide chain. In some embodiments, an anti-glyco-LAMP1 variable light chain (VL) and a CH1 domain are included in the polypeptide chain that does not include the anti-glyco-LAMP1 VH and CL. When the first and second polypeptide chains dimerize, the anti-glyco-LAMP1 VH and VL, and the CH1 and CL, are brought together to form an anti-glyco-LAMP1 Fab domain. In some embodiments, the VH and the CH1 or CL is included in the first polypeptide chain, and the VL and the CL or CH1 is included in the second polypeptide chain. In other embodiments, the VH and the CH1 or CL is included in the second polypeptide chain, and the VL and the CH1 or CL is included in the first polypeptide chain.

[0268] In other embodiments, the anti-glyco-LAMP1 VH and CH1 or CL are included in the first polypeptide chain of the second polypeptide chain, and the chimeric TCR further comprises a third polypeptide comprising the VL and either a CL domain or a CH1 domain. The third polypeptide is capable of associating with the VH and CH1 or CL of the first or second polypeptide chain, thus forming a Fab domain. In some embodiments, both the first and second polypeptide chains include a VH and a CH1 domain or a CL domain. Where both the first and second polypeptide chains include a VH and a CH1 or CL, a third polypeptide comprising a VL and a CL or CH1 associates with the first polypeptide chain to form a first Fab domain, and a fourth polypeptide comprising a VL and a CL or CH1 associates with the second polypeptide chain to form a second Fab domain.

[0269] First and second TCR domains are included in the first and second polypeptide chains, respectively, with the first TCR domain comprising a first TCR transmembrane domain from a first TCR subunit and the second TCR domain comprising a second TCR transmembrane domain from a second TCR subunit. In some embodiments, the first TCR subunit is a TCR α chain and the second TCR subunit is a TCR β chain. In other embodiments, the first TCR subunit is a TCR β chain and the second TCR subunit is a TCR α chain. In In some embodiments, the first TCR subunit is a TCR γ chain and the second TCR subunit is a TCR δ chain. In other embodiments, the first TCR subunit is a TCR δ chain and the second TCR subunit is a TCR γ chain. A TCR transmembrane domain from a TCR subunit can be a native TCR transmembrane domain, a natural or engineered variant thereof, or a fragment of the native or variant TCR transmembrane domain. In some embodiments, the first and/or second TCR transmembrane domains comprise, individually, an amino acid sequence of a TCR transmembrane domain contained in one of SEQ ID NOS:77-80 of WO 2017/070608, which is incorporated by reference in its entirety. In other embodiments, the first and/or second TCR

transmembrane domains comprise, individually, an amino acid sequence of SEQ ID NOS:1-4 of WO 2017/070608.

[0270] In some embodiments, in addition to the first and second TCR transmembrane domains, the first and second TCR domains also include first and second connecting peptides, respectively. The first and second connecting peptides are positioned at the N-terminus of the first and second TCR transmembrane domains, respectively. In some embodiments, the first connecting peptide comprises all or a portion of the connecting peptide of the first TCR subunit and/or the second connecting peptide comprises all or a portion of the connecting peptide of the second TCR subunit. In some embodiments, the first transmembrane domain and the first connecting peptide are derived from different TCR subunits and/or the second transmembrane domain and the second connecting peptide are derived from different TCR subunits. A connecting peptide from a TCR subunit can be a native TCR connecting peptide, a natural or engineered variant thereof, or a fragment of the native or variant TCR connecting peptide. In some embodiments, the first and/or second connecting peptides comprise, individually, an amino acid sequence of a connecting peptide contained in one of SEQ ID NOS:77-80 of WO 2017/070608. In other embodiments, the first and/or second connecting peptides comprise, individually, an amino acid sequence of SEQ ID NOS:5-12 of WO 2017/070608.

[0271] In some embodiments, the first and second TCR domains comprise a first and second TCR constant domain, respectively. The first and second TCR constant domains are positioned at the C-terminus of the first and second TCR transmembrane domains, respectively. If the first and/or second TCR domains include a TCR connecting peptide, the TCR constant domain can be positioned at the C-terminus of the TCR connecting peptide. In some embodiments, the first TCR constant domain comprises all or a portion of the constant domain of the first TCR subunit and/or the second TCR constant domain comprises all or a portion of the constant domain of the second TCR subunit. For example, in some embodiments, the first and/or second TCR constant domains are derived from TCR α and β subunit constant domains, or TCR γ and δ subunit constant domains. A TCR constant domain from a TCR subunit can be a native TCR intra constant cellular domain, a natural or engineered variant thereof, or a fragment of the native or variant TCR constant domain. In some embodiments, the first and/or second TCR constant domain comprise, individually an amino acid sequence of SEQ ID NOS:172, 174, 176, 178, 180, or 182, or the wildtype equivalent thereof.

[0272] In some embodiments, the first and second TCR domains comprise first and second TCR intracellular domains, respectively. The first and second TCR intracellular domains are positioned at the C-terminus of the first and second TCR transmembrane domains, respectively. In some embodiments, the first TCR intracellular domain comprises all or a portion of the intracellular domain of the first TCR subunit and/or the second TCR intracellular domain comprises all or a portion of the intracellular domain of the second TCR subunit. A TCR

intracellular domain from a TCR subunit can be a native TCR intracellular domain, a natural or engineered variant thereof, or a fragment of the native or variant TCR intracellular domain. In some embodiments, the first and/or second TCR intracellular domains comprise, individually, an amino acid sequence of a TCR intracellular domain contained in one of SEQ ID NOS:77-80 of WO 2017/070608. In other embodiments, the first and/or second TCR intracellular domain comprise, individually, an amino acid sequence of SEQ ID NOS:13-14 of WO 2017/070608.

[0273] In some embodiments, the first polypeptide chain of the chimeric TCR further comprises a first accessory intracellular domain C-terminal to the first TCR transmembrane domain and/or the second polypeptide chain of the chimeric TCR further comprises a second accessory intracellular domain C-terminal to the second transmembrane domain. In some embodiments, the first and/or second accessory intracellular domains comprise a TCR costimulatory domain. In some embodiments, the TCR costimulatory domain comprises all or a portion of the amino acid sequence of SEQ ID NO: 70 or 71 of WO 2017/070608.

[0274] In some embodiments the first TCR domain is a fragment of the first TCR subunit and/or the second TCR subunit is a fragment of the second TCR subunit.

[0275] The first and second polypeptide chains that form the chimeric TCR are linked. In some embodiments, the first and second polypeptide chains that form the chimeric TCR are linked by a disulfide bond. In some embodiments, first and second polypeptide chains that form the chimeric TCR are linked by a disulfide bond between a residue in the first connecting peptide and a residue in the second connecting peptide.

[0276] In some embodiments, the first and second polypeptide chains are linked or otherwise associate. In some embodiments, the associated first and second polypeptide chains are capable of recruiting at least one TCR-associated signaling modules, such as, *e.g.*, CD3 $\delta\epsilon$, CD3 $\gamma\epsilon$, and $\zeta\zeta$. In certain embodiments, the associated first and second polypeptide chains are capable of recruiting each of CD3 $\delta\epsilon$, CD3 $\gamma\epsilon$, and $\zeta\zeta$, forming a TCR-CD3 complex.

[0277] In some embodiments, the first polypeptide chain comprises a first linker between the first TCR domain and an anti-glyco-LAMP1 VH or VL of the scFv, Fv, or Fab fragment included in the first polypeptide chain. In some embodiments, the second polypeptide chain comprises a second linker between the second TCR domain and an anti-glyco-LAMP1 VH or VL of the scFv, Fv, or Fab fragment included in the second polypeptide chain. In some embodiments, the first peptide linker and/or the second peptide linker comprises between about 5 to about 70 amino acids. In some embodiment, the first and/or second linker comprises a constant domain or fragment thereof from an immunoglobulin or T cell receptor subunit. In some embodiments, the first and/or second linker comprises an immunoglobulin constant domain or fragment thereof. For example in those embodiments described above comprising a CH1 or CL domain, the CH1 or CL domain functions as a linker between the TCR domain and the anti-glyco-LAMP1 binding fragment, or a subpart (*e.g.*, VH or VL) thereof. The immunoglobulin constant domain can also

be, in addition to CH1 or CL, a CH2, CH3, or CH4 domain or fragment thereof. The immunoglobulin constant domains can be derived from an IgG (e.g., IgG1, IgG2, IgG3, or IgG4), IgA (e.g., IgA1 or IgA2), IgD, IgM, or IgE heavy chain. In some embodiments the constant domains can be derived from a human (e.g., IgG1, IgG2, IgG3, or IgG4), IgA (e.g., IgA1 or IgA2), IgD, IgM, or IgE heavy chain. In other embodiments, a TCR constant domain or fragment thereof described above functions as a linker between the TCR domain and the anti-glyco-LAMP1 binding fragment, or a subpart (e.g., VH or VL) thereof. In some embodiments, the first and second linkers are capable of binding to one another.

[0278] In some embodiments, the first and second polypeptide chains are connected, at least temporarily, by a cleavable peptide linker. In some embodiments, the cleavable peptide linker is a furin-p2A cleavable peptide. The cleavable peptide linker can facilitate expression of the two polypeptide chains. The cleavable peptide linker can be configured to temporarily associate the first polypeptide chain with the second polypeptide chain during and/or shortly after protein translation.

[0279] In some embodiments, the chimeric TCR is a synthetic T cell receptor and antigen receptor (STAR), as described in Liu et al., 2021, Sci Transl Med, and WO 2020/029774, the contents of each of which are incorporated herein by reference in their entireties.

[0280] In some aspects, the STAR comprises, from N- to C-terminus, a first polypeptide chain comprising an anti-glyco- LAMP1 variable heavy chain and a TCR α chain constant region domain; a cleavable peptide linker; and a second polypeptide chain comprising an anti-glyco- LAMP1 variable light chain and a TCR β constant region domain (configuration STAR 1).

[0281] In other aspects, the STAR comprises, from N- to C-terminus, a first polypeptide chain comprising an anti-glyco- LAMP1 variable heavy chain and a TCR β chain constant region domain; a cleavable peptide linker; and a second polypeptide chain comprising an anti-glyco- LAMP1 variable light chain and a TCR α constant region domain (configuration STAR 2).

[0282] In other aspects, the STAR comprises, from N- to C-terminus, a first polypeptide chain comprising an anti-glyco- LAMP1 variable light chain and a TCR α chain constant region domain; a cleavable peptide linker; and a second polypeptide chain comprising an anti-glyco- LAMP1 variable heavy chain and a TCR β constant region domain (configuration STAR 3).

[0283] In other aspects, the STAR comprises, from N- to C-terminus, a first polypeptide chain comprising an anti-glyco- LAMP1 variable light chain and a TCR β chain constant region domain; a cleavable peptide linker; and a second polypeptide chain comprising an anti-glyco- LAMP1 variable heavy chain and a TCR α constant region domain (configuration STAR 4).

[0284] In certain embodiments, the TCR α chain constant region domain and the TCR β chain constant region domain of any one of configurations STAR 1 through STAR 4 can be replaced by TCR γ and TCR δ constant region domains, respectively.

[0285] The chimeric TCRs of the present disclosure can form complexes with TCR-associated signaling molecules (e.g., CD3 $\gamma\epsilon$, CD3 $\delta\epsilon$, and $\zeta\zeta$) endogenously expressed in T cells. These complexes provide for TCR signaling controlled by binding of the anti-glyco- LAMP1 heavy and light variable chains by its target.

[0286] Chimeric TCRs of the disclosure are further described in numbered embodiments 602 to 695.

5.4.1. TCR Constant Domains

[0287] With respect to the TCR constant domains, the chimeric TCR can be designed to comprise constant regions that are derived from, e.g., human peripheral blood T cells. Nucleotide and corresponding amino acid sequences for TCR constant regions for use in chimeric TCRs according to the disclosure are provided in Table 5.

Table 5 Nucleotide and Amino Acid Sequences for TCR Constant Regions		
Description	Sequence	SEQ ID NO:
TCR α Constant Region – Nucleic Acid (human)	gatatccagaaccctgaccctgctgtctatcaactccgggactctaaatcca gtgacaagtctgtctgctattcaccgattttgattctcaacaaatgtgtcac aaagtaaggattctgtgtgtatcacagacaaatgtgtgctagacatgag gtctatggactcaagagcaacagtgtgtggcctggagcaacaaatctga ctttgcatgtgcaaacgcctcaacaacagcattattccagaagacacctct tcccagcccagaaagtctgtgtatgtaagctggcgagaaaagctttg aaacagatagcaacctaacttcaaaacctgtcagtgattgggtccgaat cctctctgaaagtggccgggttaatctgtcatgacgtgctgggtgtgtg ccagc	171
TCR α Constant Region – Amino Acid (human)	XIQNPDPVYQLRDSKSSDKSVCLFTDFDSQTNVSQS KDSDVYITDKCVLDMRSMDFKSNSAVAWSNKSDFAC ANAFNNSIIPEDTFFPSPSSCDVKLVEKSFETDTNLN FQNLSVIGFRILLKLVAGFNLLMTLRLWSS X=Asp, Asn, His, Tyr	172
TCR α Constant Region – Amino Acid (murine); Cysteine mutant	Aatatccagaaccagaaccctgctgtgtaccagttaaagatcctcggtct caggacagaccctctgctgttcaccgacttgactccaaatcaatgtgc cgaaaaccttggaatctggaacgttcactgacaaaactgtgtggac atgaaagctatggattccaagagcaatggggccattgcctggagcaacca gacaagcttcacgtccaagatacttcaagagaccaacgccacctacc ccagttcagacgttccctgtatgccacgttgactgagaaaagcttgaaac agatatgaacctaaacttcaaaacctgtcagttatgggactccgaatcctcc tgctgaaagtagccggatttaacctgtcatgacgtgaggctgtgtgctcag ttga	173
TCR α Constant Region – Amino Acid (murine); Cysteine mutant	XIQNPEPAVYQLKDPQRSQDSTLCLFTDFDSQINVPKT MESGTFITDKTVLDMKAMDSKSNAGIAWSNQTSFTC QDIFKETNATYPSSDVPCDATLTEKSFETDMNLNFQN LSVMGLRILLKLVAGFNLLMTLRLWSS X at 1, x=Asp, Asn, His, Tyr	174
TCR β Constant Region – Nucleic Acid (human)	gaggacctgaaaaacgtgttcccacccgaagtggcgtcttcgaaccatc agaagcagagatctcccacacccaaaaggccacactggtgtgctggcc acaggctcttcccagaccacgtggagctgagctggtgggtgaatgggaa ggagggtcacagtgggtctgcacagaccgcagccctcaaggagca gcccgccctcaatgactccagatactgcctgagcagccgctgagggtctc ggccaccttctggcagaaccccgcaaccacttccgtgtcaagtccagtt ctacgggctctcggaatgacgagtggaaccaggataggccaaaccc gtcaccagatcgtcagcgcgaggcctggggtagagcagactgtggcttt acctcgggtgctctaccagcaagggtcctgtctgccaccatcctcatgaga	175

Table 5 Nucleotide and Amino Acid Sequences for TCR Constant Regions		
Description	Sequence	SEQ ID NO:
	tctgctaggggaagggccaccctgtatgctgtgctggcagcgccctgtgttg atggccatgggtcaagagaaaggatttc	
TCR β Constant Region – Amino Acid (human)	EDLKNVFPPEVAVFEPSEAEISHTQKATLVCLATGFFP DHVELSWWWNGKEVHSGVCTDPQPLKEQPALNDSR YCLSSRLRVSATFWQNPRNHFRQVQFYGLSENDE WTQDRAKPVTQIVSAEAWGRADCGFTSVSYQQGV SATILYEILLGKATLYAVLVLSALVLMAMVKRKD	176
TCR β Constant Region – Amino Acid (murine); Cysteine mutant	gaggatctgagaatgtgactccacccaaggtctcctgttgagccatcaa aagcagagattgcaaacaaacaaaggctaccctcgtgtgctggccag gggtctctccctgaccacgtggagctgagctgggtggaatggcaagga ggtccacagtgggtgagcagcgacccctcaggcctacaaggagagcaat tatagtactgctgagcagcgctgagggctctgctacctctggcaca atcctcgcaaccacttcgctgccaagtgcagttccatgggcttcagagga ggacaagtggccagagggtcaccacaaacctgtcacacagaacatcagt gcagaggcctggggccgagcagactgtgggattacctcagcatcctatca acaaggggtctgtgctgccaccatcctctatgagatcctgtagggaaagcc accctgtatgctgtgctgctgtagtacactggtggtgatggctatggtcaaaag aagaattca	177
TCR β Constant Region – Amino Acid (murine); Cysteine mutant	EDLRNVTPPKVSLFEP SKAEIANKQKATLVCLARGFFP DHVELSWWWNGKEVHSGVSTDPQAYKESNYSYCLS SRLRVSATFWHNP RNHFRCQVQFHGLSEEDKWPEG SPKPV TQNISAEAWGRADCGITSASYQQGVLSATILY EILLGKATLYAVLVSTLVVMAMVKRKNS	178
TCR γ Constant Region – Amino Acid (human)	DKQLDADVSPKPTIFLPSIAETKLQKAGTYLCLLEKFFP DVIKIHWQEKKSNITLGSQEGNTMKTNDTYMKFSWLT VPEKSLDKEHRCIVRHENNKNGVDQEIIFFPIKTDVITM DPKDNC SKDANDTLLLQLTNTSAYMYLLLLLKS VVY FAITCCLLRRTAFCCNGEKS	179
TCR γ Constant Region – Amino Acid (murine)	XKRLDADISPKPTIFLPSVAETNLHKTGTYLCLLEKFFP DVIRVYWKEKDGNTILDSQEGDTLKTNDTYMKFSWLT VPERAMGKEHRCIVKHENNKGGADQEIFFPSIKK VAV STKPTTCWQDKNDVLQLQFTITSAYTYLLLLLKS VIYL AIISFLLRRTSVCGNEKKS X = any naturally occurring amino acid	180
TCR δ Constant Region – Amino Acid (human)	SQPHTKPSVFMKNGTNVACL VKEFY PKDIRINLVSS KKITEFDPAIVISPSGKYNAVKLGKYEDSNSVTCSVQH DNKTVHSTD FEVKT DSTDHVKPKETENTKQPSKSCH KPKAIVHTEKVNMMSLTVLGLRMLFAKT VAVNFLTAK LFFL	181
TCR δ Constant Region – Amino Acid (murine)	XSQPPAKPSVFMKNGTNVACL VKDFYPKEVTISLRSS KKIVEFDPAIVISPSGKYSAVKLGQYGDSNSVTCSVQH NSETVHSTD FEPYANSFNNEKLPEPENDTQISEPCY GPRVTVHTEKVNMMSLTVLGLRLLFAKT IAINFLT VKLF F X = any naturally occurring amino acid	182

[0288] In certain embodiments the TCR constant domain of the chimeric TCR can be modified to provide for additional bonds between two TCR constant domains of the chimeric TCR. In some embodiments, the residue corresponding to position 48 of the wildtype human TCR α constant domain is mutated to cysteine and the residue corresponding to position 57 of the wildtype human TCR β constant domain is mutated to cysteine, as shown in Table 5. This results in the formation of a disulfide linkage between TCR α and TCR β constant domains,

resulting in a disulfide bond between the first and second polypeptide chains of the chimeric TCR. In some embodiments, the residue corresponding to position 85 of the wildtype human TCR α constant domain is mutated to alanine and the residue corresponding to position 88 of the wildtype human TCR β constant domain is mutated to glycine, as shown in Table 5. Again, this results in the formation of a disulfide linkage between TCR α and TCR β constant regions.

5.4.2. Cleavable Linkers

[0289] In some embodiments, the two polypeptide chains of the chimeric TCRs of the disclosure are linked via a cleavable peptide linker. In some embodiments, the two polypeptide chains of the chimeric TCR are linked via a furin-P2A peptide linker, which provides a protease cleavage site between the two polypeptide chains. The two polypeptide chains can thus be transcribed and translated into a fusion protein, which is subsequently cleaved by a protease into two distinct protein subunits. In some embodiments, the two resulting protein subunits are covalently bound through disulfide bonds, and subsequently form a complex with the endogenous CD3 subunits of T cells.

[0290] In some embodiments, the furin-P2A peptide linker comprises the sequence RAKRSGSGATNFSLLKQAGDVEENPGP (SEQ ID NO:183).

[0291] In some embodiments, the furin-P2A peptide linker comprises the sequence ATNFSLLKQAGDVEENPGP (SEQ ID NO:184).

5.5 Neuraminidase

[0292] Sialic acids are terminal sugars of glycans on either glycoproteins or glycolipids on the cell surface, and have been shown to be aberrantly expressed during tumor transformation and malignant progression. Hypersialylation frequently occurs in tumor tissues due to aberrant expression of sialyltransferases/sialidases. This can result in accelerated cancer progression. Sialylation facilitates immune escape, enhances tumor proliferation and metastasis, helps tumor angiogenesis, and assists in resisting apoptosis and cancer therapy.

[0293] Host cells (e.g., T cells, NK cells) expressing a CAR of the disclosure can be engineered to coexpress a cell surface or secreted neuraminidase (sialidase) along with the CAR. The cell surface neuraminidase, anchored to the cell surface via a heterologous transmembrane, gives the host cell glycoediting activity. This enhances cytotoxic effects and anti-tumor efficacy of the CAR-T cell and immune cells such as innate NK cells and monocytes. Host cells coexpressing a CAR and an engineered neuraminidase are described in PCT Publication No WO2020/236964, which is incorporated herein by reference in its entirety.

[0294] A neuraminidase can be coexpressed in a host cell along with a CAR described herein. Exemplary host cells coexpressing a neuraminidase and a CAR are described in the specific embodiments.

[0295] The neuraminidase can be included as a domain of a fusion protein described herein.

[0296] In certain embodiments, the neuraminidase is EC 3.2.1.18 or EC 3.2.1.129.

[0297] In some embodiments, the neuraminidase is derived from *Micromonospora viridifaciens*.

[0298] In some aspects, the neuraminidase comprises an amino acid sequence having at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to:

GGSPVPPGGEPLYTEQDLAVNGREGFPNYRIPALTVTPDGDLLASYDGRPTGIDAPGPNLSILQ
RRSTDGGRTWGEQQVVSAGQTTAPIKGFSDPSYLVRETGTIFNFHVYSQRQGFAGSRPGTD
PADPNVLHANVATSTDGGLTWSHRTITADITPDGWRSRFAASGEGIQRLRYGPHAGRLIQYTI
INAAGAFQAVSVYSDDHGRTWRAGEAVGVGMDENKTVELSDGRVLLNSRDSARSQGYRKVAV
STDGGHSYGPVTIDRLPDPTNNASIIRAFPDAPAGSARAKVLLFSNAASQTSRSQGTIRMSCD
DGQTPVPSKVFQPGSMSYSTLTALPDGTYGLLYEPGTGIRYANFNLAWLGG (SEQ ID NO:
210).

[0299] The neuraminidase can be retained at a surface of a host cell engineered to express the neuraminidase, or can be secreted by a host cell engineered to express the neuraminidase. The host cell engineered to express the neuraminidase can include, for example, a vector encoding the neuraminidase.

5.6 MicAbodies

[0300] The present disclosure provides MicAbodies comprising the anti-glyco-LAMP1 antibodies and antigen-binding fragments of the disclosure. MicAbodies are fusion proteins comprising an antibody or antigen-binding fragment and an engineered MHC-class I-chain-related (MIC) protein domain. MIC proteins are the natural ligands of human NKG2D receptors expressed on the surface of NK cells, and the α 1- α 2 domain of MIC proteins provides the binding site for the NKG2D receptor. By fusing an engineered MIC protein domain (e.g. an engineered α 1- α 2 domain) to a cancer-targeting antibody or antigen-binding fragment, T-cells expressing an engineered NKG2D receptor capable of binding the engineered MIC protein domain can be targeted to cancer cells. Engineered MIC protein domains that can be included in MicAbodies of the disclosure, and NKG2D receptors capable of binding the engineered MIC protein domains, CARs and CAR T cells comprising the NKG2D receptors are described in U.S. publication nos. US 2011/0183893, US2011/0311561, US 2015/0165065, and US 2016/0304578 and PCT publication nos. WO 2016/090278, WO 2017/024131, WO 2017/222556, and WO 2019/191243, the contents of which are incorporated herein by reference in their entireties.

[0301] In some embodiments, the MicAbodies of the disclosure comprise α 1- α 2 domains which are at least 80% identical or homologous to the α 1- α 2 domain of an NKG2D ligand (e.g., MICA, MICB, ULBP1, ULBP2, ULBP3, ULBP4, ULBP5, ULBP6, or OMCP). Exemplary amino acid sequences of MICA, MICB, ULBP1, ULBP2, ULBP3, ULBP4, ULBP5, ULBP6, and OMCP are

set forth as SEQ ID NOS: 1-9 of WO 2019/191243, respectively, the sequences of which are incorporated herein by reference. In other embodiments, the $\alpha 1$ - $\alpha 2$ domain is 85% identical to a native or natural $\alpha 1$ - $\alpha 2$ domain of an NKG2D ligand. In yet other embodiments, the $\alpha 1$ - $\alpha 2$ domain is 90% identical to a native or natural $\alpha 1$ - $\alpha 2$ domain of a natural NKG2D ligand protein and binds non-natural NKG2D.

[0302] In some embodiments, the MicAbodies of the disclosure comprise $\alpha 1$ - $\alpha 2$ domains which are at least 80% identical or homologous to a native or natural $\alpha 1$ - $\alpha 2$ domain of a human MICA or MICB protein and bind NKG2D. In some embodiments, the $\alpha 1$ - $\alpha 2$ domain is 85% identical to a native or natural $\alpha 1$ - $\alpha 2$ domain of a human MICA or MICB protein and binds NKG2D. In other embodiments, the $\alpha 1$ - $\alpha 2$ domain is 90%, 95%, 96%, 97%, 98%, or 99% identical to a native or natural $\alpha 1$ - $\alpha 2$ platform domain of a human MICA or MICB protein and binds NKG2D.

[0303] In some embodiments, specific mutations in $\alpha 1$ - $\alpha 2$ domains of NKG2D ligands can be made to create non-natural $\alpha 1$ - $\alpha 2$ domains that bind non-natural NKG2D receptors, themselves engineered so as to have reduced affinity for natural NKG2D ligands. This can be done, for example, through genetic engineering. A non-natural NKG2D receptor so modified can be used to create on the surface of NK- or T-cells of the immune system an NKG2D-based CAR that can preferentially bind to and be activated by molecules comprised of the non-natural $\alpha 1$ - $\alpha 2$ domains. These pairs of non-natural NKG2D receptors and their cognate non-natural NKG2D ligands can provide important safety, efficacy, and manufacturing advantages for treating cancer and viral infections as compared to traditional CAR-T cells and CAR-NK cells. Activation of CAR-T cells and CAR-NK cells having a NKG2D-based CAR can be controlled by administration of a MicAbody. In the event that an adverse event develops, the dosing regimen of the MicAbody can be modified rather than having to deploy an induced suicide mechanism to destroy the infused CAR cells.

[0304] MicAbodies can be generated by attaching an antibody or antigen-binding fragment to an engineered $\alpha 1$ - $\alpha 2$ domain via a linker, e.g., APTSSSGGGGS (SEQ ID NO:185), GGGGS (SEQ ID NO:186), or GGGGS (SEQ ID NO:159). For example, an $\alpha 1$ - $\alpha 2$ domain can be fused to the C-terminus of an IgG heavy chain or light chain, for example, as described in WO 2019/191243.

[0305] In some embodiments, the MicAbodies of the disclosure comprise an engineered $\alpha 1$ - $\alpha 2$ domain comprising the amino acid sequence
EPHSLRYNLTVLSWDGSGFLTEVHLDGQPFLRCRQKCRAPQGQWAEDVLGNKTWD
RETRDLTGWGTLLMTLAHIKDQKEGLHSLQEIRVCEIHEDNSTRSSQHFYYDGELFLSQNLET
LEWTMPQSSRAQTLAMNVRNFLKEDAMETDIGYRLMRADCLSELRRYLKSGVVLRRTV (SEQ ID NO:187) (MICA25.17).

[0306] In other embodiments, the MicAbodies of the disclosure comprise an engineered $\alpha 1$ - $\alpha 2$ domain comprising the amino acid sequence

EPHSLRYNLTVLSWDGSVQSGFLTEVHLDGQPFLRCRQKCRAPQGGQWAEDVLGNKTWD
RETRDLTGWGTFLRMTLAHIKDQKEGLHSLQEIRVCEIHEDNSTRSSQHFYYDGELFLSQNLET
LEWTMPQSSRAQTLAMNVRNFLKEDAMETDRSGLLMRADCLSELRRYLKSGVVLRRTV (SEQ
ID NO:215) (MICA25.18).

[0307] In other embodiments, the MicAbodies of the disclosure comprise an engineered $\alpha 1$ - $\alpha 2$ domain comprising the amino acid sequence

AAEPHLSYDITVIPKFRPGPRWCAVQGGQVDEKTFLLHYDCGNKTVTPVSPLGKKLNVTAWKA
QNPVLREVVDILTEQLWDIQLENYTPKEPLTLQARMSCEQKAEGHSSGSWQFSFDGQIFLLFD
SEKRMWTTVHPGARKMKEKWENDKVVATTLYTWSMGDCIGWLEDFLMGMDSTLEPSAGAP
(SEQ ID NO:188) (ULBP2.S1).

[0308] In other embodiments, the MicAbodies of the disclosure comprise an engineered $\alpha 1$ - $\alpha 2$ domain comprising the amino acid sequence

AAEPHLSYDITVIPKFRPGPRWCAVQGGQVDEKTFLLHYDCGNKTVTPVSPLGKKLNVTAWKA
QNPVLREVVDILTEQLWDIQLENYTPKEPLTLQARMSCEQKAEGHSSGSWQFSFDGQIFLLFD
SEKRMWTTVHPGARKMKEKWENDKVVATLMRIWSMGDCIGWLEDFLMGMDSTLEPSAGAP
(SEQ ID NO:189) (ULBP2.S2).

[0309] In other embodiments, the MicAbodies of the disclosure comprise an engineered $\alpha 1$ - $\alpha 2$ domain comprising the amino acid sequence

AAEPHLSYDITVIPKFRPGPRWCAVQGGQVDEKTFLLHYDCGNKTVTPVSPLGKKLNVTAWKA
QNPVLREVVDILTEQLWDIQLENYTPKEPLTLQARMSCEQKAEGHSSGSWQFSFDGQIFLLFD
SEKRMWTTVHPGARKMKEKWENDKVVATKLYLWSMGDCIGWLEDFLMGMDSTLEPSAGAP
(SEQ ID NO:190) (ULBP2.S3).

[0310] In other embodiments, the MicAbodies of the disclosure comprise an engineered $\alpha 1$ - $\alpha 2$ domain comprising the amino acid sequence

AAEPHSLWYNFTIIHLPRHGQQWCEVQSQVDQKNFLSYDCGSDKVLSMGHLEEQLYATDAW
GKQLEMLREVGQRLRLELADTELEDFTPSGPLTLQVRMSCESEADGYIRGSWQFSFDGRKFL
LFDSNNRKWTVHAGARRMKEKWEKDSGLTTDLIRSMGDCKSWLRDFLMHRKKRLEPTAP
(SEQ ID NO:191) (ULBP3.S1).

[0311] In other embodiments, the MicAbodies of the disclosure comprise an engineered $\alpha 1$ - $\alpha 2$ domain comprising the amino acid sequence

AAEPHSLWYNFTIIHLPRHGQQWCEVQSQVDQKNFLSYDCGSDKVLSMGHLEEQLYATDAW
GKQLEMLREVGQRLRLELADTELEDFTPSGPLTLQVRMSCESEADGYIRGSWQFSFDGRKFL
LFDSNNRKWTVHAGARRMKEKWEKDSGLTTYFYLRSMGDCKSWLRDFLMHRKKRLEPTAP
(SEQ ID NO:192) (ULBP3.S2).

[0312] In other embodiments, the MicAbodies of the disclosure comprise an engineered $\alpha 1$ - $\alpha 2$ domain comprising the amino acid sequence

EPHSLSYDITVIPKFRPGPRWCAVQGQVDEKTFLLHYDCGNKTVTPVSPLGKKLNVTTAWKAQN
PVLREVVDILTEQLWDIQLENYTPKEPLTLQARMSCEQKAEGHSSGSWQFSFDGQIFLLFDSE
KRMWTTVHPGARKMKEKWENDKVVATILWQTSMGDCIGWLEDFLMGMDSTLEPS (SEQ ID
NO:193) (ULBP2.C).

[0313] In other embodiments, the MicAbodies of the disclosure comprise an engineered $\alpha 1$ - $\alpha 2$ domain comprising the amino acid sequence

EPHSLSYDITVIPKFRPGPRWCAVQGQVDEKTFLLHYDCGNKTVTPVSPLGKKLNVTTAWKAQN
PVLREVVDILTEQLWDIQLENYTPKEPLTLQARMSCEQKAEGHSSGSWQFSFDGQIFLLFDSE
KRMWTTVHPGARKMKEKWENDKVVATLLWGWWSMGDCIGWLEDFLMGMDSTLEPS (SEQ ID
NO:194) (ULBP2.R).

[0314] In other embodiments, the MicAbodies of the disclosure comprise an engineered $\alpha 1$ - $\alpha 2$ domain comprising the amino acid sequence

EPHSLSYDITVIPKFRPGPRWCAVQGQVDEKTFLLHYDCGNKTVTPVSPLGKKLNVTTAWKAQN
PVLREVVDILTEQLWDIQLENYTPKEPLTLQARMSCEQKAEGHSSGSWQFSFDGQIFLLFDSE
KRMWTTVHPGARKMKEKWENDKVVATMFWSWSMGDCIGWLEDFLMGMDSTLEPS (SEQ ID
NO:195) (ULBP2.AA).

[0315] In other embodiments, the MicAbodies of the disclosure comprise an engineered $\alpha 1$ - $\alpha 2$ domain comprising the amino acid sequence

EPHSLSYDITVIPKFRPGPRWCAVQGQVDEKTFLLHYDCGNKTVTPVSPLGKKLNVTTAWKAQN
PVLREVVDILTEQLWDIQLENYTPKEPLTLQARMSCEQKAEGHSSGSWQFSFDGQIFLLFDSE
KRMWTTVHPGARKMKEKWENDKVVATLMWQWSMGDCIGWLEDFLMGMDSTLEPS (SEQ ID
NO:196) (ULBP2.AB).

[0316] An exemplary engineered NKG2D receptor comprises the amino acid sequence

NSLNFNQEVIPLTESYCGPCPNWICYKNNCYQFFDESKNWWYESQASCMSQNASLLKVYSKE
DQDLLKLKLSYHWMGLVHIPTNGSWQWEDGSILSPNLLTIEMQKGDALYASSFKGYIENCST
PNTYICMQRTV (SEQ ID NO:197) in which the tyrosine at position 73 has been replaced with
another amino acid, for example alanine.

[0317] Another exemplary engineered NKG2D receptor comprises the amino acid sequence

FLNSLNFNQEVIPLTESYCGPCPNWICYKNNCYQFFDESKNWWYESQASCMSQNASLLKVYS
KEDQDLLKLKLSYHWMGLVHIPTNGSWQWEDGSILSPNLLTIEMQKGDALYASSFKGYIENC
STPNTYICMQRTV (SEQ ID NO:198) in which the tyrosines at positions 75 and 122 have
been replaced with another amino acid, for example alanine at position 75 and phenylalanine at
position 122.

5.7 Nucleic Acids, Recombinant Vectors and Host Cells

[0318] The present disclosure encompasses nucleic acid molecules encoding immunoglobulin light and heavy chain genes for anti-glyco-LAMP1 antibodies, vectors comprising such nucleic

acids, and host cells capable of producing the anti-glyco-LAMP1 antibodies of the disclosure. In certain aspects, the nucleic acid molecules encode, and the host cells are capable of expressing, the anti-glyco-LAMP1 antibodies and antibody-binding fragments of the disclosure (e.g., as described in Section 5.1 and numbered embodiments 1 to 526) as well as fusion proteins (e.g., as described in numbered embodiments 533 to 557), and chimeric antigen receptors (e.g., as described in Section 5.3 and numbered embodiments 558 to 591) and chimeric T cell receptors (e.g., as described in Section 5.4 and numbered embodiments 602 to 695) containing them. Exemplary vectors of the disclosure are described in numbered embodiments 698 to 700 and exemplary host cells are described in numbered embodiments 701 to 707.

[0319] An anti-glyco-LAMP1 antibody of the disclosure can be prepared by recombinant expression of immunoglobulin light and heavy chain genes in a host cell. To express an antibody recombinantly, a host cell is transfected with one or more recombinant expression vectors carrying DNA fragments encoding the immunoglobulin light and heavy chains of the antibody such that the light and heavy chains are expressed in the host cell and, optionally, secreted into the medium in which the host cells are cultured, from which medium the antibodies can be recovered. Standard recombinant DNA methodologies are used to obtain antibody heavy and light chain genes, incorporate these genes into recombinant expression vectors and introduce the vectors into host cells, such as those described in *Molecular Cloning: A Laboratory Manual*, Second Edition (Sambrook, Fritsch and Maniatis (eds), Cold Spring Harbor, N. Y., 1989), *Current Protocols in Molecular Biology* (Ausubel, F. M. *et al.*, eds., Greene Publishing Associates, 1989) and in U.S. Pat. No. 4,816,397.

[0320] To generate nucleic acids encoding such anti-glyco-LAMP1 antibodies, DNA fragments encoding the light and heavy chain variable regions are first obtained. These DNAs can be obtained by amplification and modification of germline DNA or cDNA encoding light and heavy chain variable sequences, for example using the polymerase chain reaction (PCR). Germline DNA sequences for human heavy and light chain variable region genes are known in the art (see, e.g., the “VBASE” human germline sequence database; see also Kabat *et al.*, 1991, *Sequences of Proteins of Immunological Interest*, Fifth Edition, U.S. Department of Health and Human Services, NIH Publication No. 91-3242; Tomlinson *et al.*, 1992, *J. Mol. Biol.* 22T:116-198; and Cox *et al.*, 1994, *Eur. J. Immunol.* 24:827-836; the contents of each of which are incorporated herein by reference).

[0321] Once DNA fragments encoding anti-glyco-LAMP1 antibody-related V_H and V_L segments are obtained, these DNA fragments can be further manipulated by standard recombinant DNA techniques, for example to convert the variable region genes to full-length antibody chain genes, to Fab fragment genes or to a scFv gene. In these manipulations, a V_H- or V_L-encoding DNA fragment is operatively linked to another DNA fragment encoding another protein, such as

an antibody constant region or a flexible linker. The term "operatively linked," as used in this context, is intended to mean that the two DNA fragments are joined such that the amino acid sequences encoded by the two DNA fragments remain in-frame.

[0322] The isolated DNA encoding the V_H region can be converted to a full-length heavy chain gene by operatively linking the V_H-encoding DNA to another DNA molecule encoding heavy chain constant regions (CH₁, CH₂, CH₃ and, optionally, CH₄). The sequences of human heavy chain constant region genes are known in the art (see, e.g., Kabat *et al.*, 1991, Sequences of Proteins of Immunological Interest, Fifth Edition, U.S. Department of Health and Human Services, NIH Publication No. 91-3242) and DNA fragments encompassing these regions can be obtained by standard PCR amplification. The heavy chain constant region can be an IgG₁, IgG₂, IgG₃, IgG₄, IgA, IgE, IgM or IgD constant region, but in certain embodiments is an IgG₁ or IgG₄ constant region. For a Fab fragment heavy chain gene, the V_H-encoding DNA can be operatively linked to another DNA molecule encoding only the heavy chain CH1 constant region.

[0323] The isolated DNA encoding the V_L region can be converted to a full-length light chain gene (as well as a Fab light chain gene) by operatively linking the V_L-encoding DNA to another DNA molecule encoding the light chain constant region, CL. The sequences of human light chain constant region genes are known in the art (see, e.g., Kabat *et al.*, 1991, Sequences of Proteins of Immunological Interest, Fifth Edition, U.S. Department of Health and Human Services, NIH Publication No. 91-3242) and DNA fragments encompassing these regions can be obtained by standard PCR amplification. The light chain constant region can be a kappa or lambda constant region, but in certain embodiments is a kappa constant region.

[0324] To create a scFv gene, the V_H- and V_L-encoding DNA fragments can be operatively linked to another fragment encoding a flexible linker, e.g., encoding the amino acid sequence (Gly₄~Ser)₃, such that the V_H and V_L sequences can be expressed as a contiguous single-chain protein, with the V_H and V_L regions joined by the flexible linker (see, e.g., Bird *et al.*, 1988, Science 242:423-426; Huston *et al.*, 1988, Proc. Natl. Acad. Sci. USA 85:5879-5883; McCafferty *et al.*, 1990, Nature 348:552-554).

[0325] To express the anti-glyco-LAMP1 antibodies of the disclosure, DNAs encoding partial or full-length light and heavy chains, obtained as described above, are inserted into expression vectors such that the genes are operatively linked to transcriptional and translational control sequences. In this context, the term "operatively linked" is intended to mean that an antibody gene is ligated into a vector such that transcriptional and translational control sequences within the vector serve their intended function of regulating the transcription and translation of the antibody gene. The expression vector and expression control sequences are chosen to be compatible with the expression host cell used. The antibody light chain gene and the antibody

heavy chain gene can be inserted into separate vectors or, more typically, both genes are inserted into the same expression vector.

[0326] The antibody genes are inserted into the expression vector by standard methods (e.g., ligation of complementary restriction sites on the antibody gene fragment and vector, or blunt end ligation if no restriction sites are present). Prior to insertion of the anti-glyco-LAMP1 antibody-related light or heavy chain sequences, the expression vector can already carry antibody constant region sequences. For example, one approach to converting the anti-glyco-LAMP1 monoclonal antibody-related V_H and V_L sequences to full-length antibody genes is to insert them into expression vectors already encoding heavy chain constant and light chain constant regions, respectively, such that the V_H segment is operatively linked to the CH segment(s) within the vector and the V_L segment is operatively linked to the CL segment within the vector. Additionally or alternatively, the recombinant expression vector can encode a signal peptide that facilitates secretion of the antibody chain from a host cell. The antibody chain gene can be cloned into the vector such that the signal peptide is linked in-frame to the amino terminus of the antibody chain gene. The signal peptide can be an immunoglobulin signal peptide or a heterologous signal peptide (*i.e.*, a signal peptide from a non-immunoglobulin protein).

[0327] In addition to the antibody chain genes, the recombinant expression vectors of the disclosure carry regulatory sequences that control the expression of the antibody chain genes in a host cell. The term “regulatory sequence” is intended to include promoters, enhancers and other expression control elements (e.g., polyadenylation signals) that control the transcription or translation of the antibody chain genes. Such regulatory sequences are described, for example, in Goeddel, *Gene Expression Technology: Methods in Enzymology* 185, Academic Press, San Diego, Calif., 1990. It will be appreciated by those skilled in the art that the design of the expression vector, including the selection of regulatory sequences may depend on such factors as the choice of the host cell to be transformed, the level of expression of protein desired, *etc.* Suitable regulatory sequences for mammalian host cell expression include viral elements that direct high levels of protein expression in mammalian cells, such as promoters and/or enhancers derived from cytomegalovirus (CMV) (such as the CMV promoter/enhancer), Simian Virus 40 (SV40) (such as the SV40 promoter/enhancer), adenovirus, (e.g., the adenovirus major late promoter (AdMLP)) and polyoma. For further description of viral regulatory elements, and sequences thereof, see, e.g., U.S. Pat. No. 5,168,062 by Stinski, U.S. Pat. No. 4,510,245 by Bell *et al.*, and U.S. Pat. No. 4,968,615 by Schaffner *et al.*

[0328] In addition to the antibody chain genes and regulatory sequences, the recombinant expression vectors of the disclosure can carry additional sequences, such as sequences that regulate replication of the vector in host cells (e.g., origins of replication) and selectable marker genes. The selectable marker gene facilitates selection of host cells into which the vector has

been introduced (see, e.g., U.S. Pat. Nos. 4,399,216, 4,634,665 and 5,179,017, all by Axel *et al.*). For example, typically the selectable marker gene confers resistance to drugs, such as G418, hygromycin or methotrexate, on a host cell into which the vector has been introduced. Suitable selectable marker genes include the dihydrofolate reductase (DHFR) gene (for use in DHFR⁻ host cells with methotrexate selection/amplification) and the neo gene (for G418 selection). For expression of the light and heavy chains, the expression vector(s) encoding the heavy and light chains is transfected into a host cell by standard techniques. The various forms of the term “transfection” are intended to encompass a wide variety of techniques commonly used for the introduction of exogenous DNA into a prokaryotic or eukaryotic host cell, e.g., electroporation, lipofection, calcium-phosphate precipitation, DEAE--dextran transfection and the like.

[0329] It is possible to express the antibodies of the disclosure in either prokaryotic or eukaryotic host cells. In certain embodiments, expression of antibodies is performed in eukaryotic cells, e.g., mammalian host cells, of optimal secretion of a properly folded and immunologically active antibody. Exemplary mammalian host cells for expressing the recombinant antibodies of the disclosure include Chinese Hamster Ovary (CHO cells) (including DHFR⁻ CHO cells, described in Urlaub and Chasin, 1980, Proc. Natl. Acad. Sci. USA 77:4216-4220, used with a DHFR selectable marker, e.g., as described in Kaufman and Sharp, 1982, Mol. Biol. 159:601-621), NSO myeloma cells, COS cells and SP2 cells. When recombinant expression vectors encoding antibody genes are introduced into mammalian host cells, the antibodies are produced by culturing the host cells for a period of time sufficient to allow for expression of the antibody in the host cells or secretion of the antibody into the culture medium in which the host cells are grown. Antibodies can be recovered from the culture medium using standard protein purification methods. Host cells can also be used to produce portions of intact antibodies, such as Fab fragments or scFv molecules. It is understood that variations on the above procedure are within the scope of the present disclosure. For example, it can be desirable to transfect a host cell with DNA encoding either the light chain or the heavy chain (but not both) of an anti-glyco-LAMP1 antibody of this disclosure.

[0330] For expression of a CAR of the disclosure, for example as described in Section 5.3 and in numbered embodiments 558 to 591, it is preferable that the host cell is a T cell, preferably a human T cell. In some embodiments, the host cell exhibits an anti-tumor immunity when the cell is cross-linked with LAMP1 on a tumor cell. Detailed methods for producing the T cells of the disclosure are described in Section 5.7.1.

[0331] For expression of a chimeric TCR of the disclosure, for example as described in Section 5.4 and in numbered embodiments 602 to 695, it is preferable that the host cell is a T cell, preferably a human T cell. In some embodiments, the host cell exhibits an anti-tumor immunity

when the cell is cross-linked with glyco-LAMP1 on a tumor cell. Detailed methods for producing the T cells of the disclosure are described in Section 5.7.1.

[0332] Recombinant DNA technology can also be used to remove some or all of the DNA encoding either or both of the light and heavy chains that is not necessary for binding to glyco-LAMP1. The molecules expressed from such truncated DNA molecules are also encompassed by the antibodies of the disclosure.

[0333] For recombinant expression of an anti-glyco-LAMP1 antibody of the disclosure, the host cell can be co-transfected with two expression vectors of the disclosure, the first vector encoding a heavy chain derived polypeptide and the second vector encoding a light chain derived polypeptide. The two vectors can contain identical selectable markers, or they can each contain a separate selectable marker. Alternatively, a single vector can be used which encodes both heavy and light chain polypeptides.

[0334] Once a nucleic acid encoding one or more portions of an anti-glyco-LAMP1 antibody, further alterations or mutations can be introduced into the coding sequence, for example to generate nucleic acids encoding antibodies with different CDR sequences, antibodies with reduced affinity to the Fc receptor, or antibodies of different subclasses.

[0335] The anti-glyco-LAMP1 antibodies of the disclosure can also be produced by chemical synthesis (*e.g.*, by the methods described in Solid Phase Peptide Synthesis, 2nd ed., 1984 The Pierce Chemical Co., Rockford, Ill.). Variant antibodies can also be generated using a cell-free platform (see, *e.g.*, Chu *et al.*, Biochemia No. 2, 2001 (Roche Molecular Biologicals) and Murray *et al.*, 2013, Current Opinion in Chemical Biology, 17:420-426).

[0336] Once an anti-glyco-LAMP1 antibody of the disclosure has been produced by recombinant expression, it can be purified by any method known in the art for purification of an immunoglobulin molecule, for example, by chromatography (*e.g.*, ion exchange, affinity, and sizing column chromatography), centrifugation, differential solubility, or by any other standard technique for the purification of proteins. Further, the anti-glyco-LAMP1 antibodies of the present disclosure and/or binding fragments can be fused to heterologous polypeptide sequences described herein or otherwise known in the art to facilitate purification.

[0337] Once isolated, the anti-glyco-LAMP1 antibody can, if desired, be further purified, *e.g.*, by high performance liquid chromatography (see, *e.g.*, Fisher, Laboratory Techniques In Biochemistry And Molecular Biology, Work and Burdon, eds., Elsevier, 1980), or by gel filtration chromatography on a Superdex™ 75 column (Pharmacia Biotech AB, Uppsala, Sweden).

5.7.1. Recombinant Production of CARs and Chimeric TCRs in T Cells

[0338] In some embodiments, nucleic acids encoding the anti-glyco-LAMP1 CARs or chimeric TCRs of the disclosure are delivered into cells using a retroviral or lentiviral vector. CAR- or chimeric TCR-expressing retroviral and lentiviral vectors can be delivered into different types of

eukaryotic cells as well as into tissues and whole organisms using transduced cells as carriers or cell-free local or systemic delivery of encapsulated, bound or naked vectors. The method used can be for any purpose where stable expression is required or sufficient.

[0339] In other embodiments, the CAR or chimeric TCR sequences are delivered into cells using *in vitro* transcribed mRNA. *In vitro* transcribed mRNA CAR or chimeric TCR can be delivered into different types of eukaryotic cells as well as into tissues and whole organisms using transfected cells as carriers or cell-free local or systemic delivery of encapsulated, bound or naked mRNA. The method used can be for any purpose where transient expression is required or sufficient.

[0340] In another embodiment, the desired CAR or chimeric TCR can be expressed in the cells by way of transposons.

[0341] One advantage of RNA transfection methods of the disclosure is that RNA transfection is essentially transient and a vector-free: an RNA transgene can be delivered to a lymphocyte and expressed therein following a brief *in vitro* cell activation, as a minimal expressing cassette without the need for any additional viral sequences. Under these conditions, integration of the transgene into the host cell genome is unlikely. Cloning of cells is not necessary because of the efficiency of transfection of the RNA and its ability to uniformly modify the entire lymphocyte population.

[0342] Genetic modification of T cells with *in vitro*-transcribed RNA (IVT-RNA) makes use of two different strategies both of which have been successively tested in various animal models. Cells are transfected with *in vitro*-transcribed RNA by means of lipofection or electroporation. Preferably, it is desirable to stabilize IVT-RNA using various modifications in order to achieve prolonged expression of transferred IVT-RNA.

[0343] Some IVT vectors are known in the literature which are utilized in a standardized manner as template for *in vitro* transcription and which have been genetically modified in such a way that stabilized RNA transcripts are produced. Currently protocols used in the art are based on a plasmid vector with the following structure: a 5' RNA polymerase promoter enabling RNA transcription, followed by a gene of interest which is flanked either 3' and/or 5' by untranslated regions (UTR), and a 3' polyadenyl cassette containing 50-70 A nucleotides. Prior to *in vitro* transcription, the circular plasmid is linearized downstream of the polyadenyl cassette by type II restriction enzymes (recognition sequence corresponds to cleavage site). The polyadenyl cassette thus corresponds to the later poly(A) sequence in the transcript. As a result of this procedure, some nucleotides remain as part of the enzyme cleavage site after linearization and extend or mask the poly (A) sequence at the 3' end. It is not clear, whether this nonphysiological overhang affects the amount of protein produced intracellularly from such a construct.

[0344] RNA has several advantages over more traditional plasmid or viral approaches. Gene expression from an RNA source does not require transcription and the protein product is produced rapidly after the transfection. Further, since the RNA has to only gain access to the cytoplasm, rather than the nucleus, and therefore typical transfection methods result in an extremely high rate of transfection. In addition, plasmid-based approaches require that the promoter driving the expression of the gene of interest be active in the cells under study.

[0345] In another aspect, the RNA construct can be delivered into the cells by electroporation. See, e.g., the formulations and methodology of electroporation of nucleic acid constructs into mammalian cells as taught in US 2004/0014645, US 2005/0052630A1, US 2005/0070841A1, US 2004/0059285A1, US 2004/0092907A1. The various parameters including electric field strength required for electroporation of any known cell type are generally known in the relevant research literature as well as numerous patents and applications in the field. See e.g., U.S. Pat. No. 6,678,556, U.S. Pat. No. 7,171,264, and U.S. Pat. No. 7,173,116. Apparatus for therapeutic application of electroporation are available commercially, e.g., the MedPulser™ DNA Electroporation Therapy System (Inovio/Genetronics, San Diego, Calif.), and are described in patents such as U.S. Pat. No. 6,567,694; U.S. Pat. No. 6,516,223, U.S. Pat. No. 5,993,434, U.S. Pat. No. 6,181,964, U.S. Pat. No. 6,241,701, and U.S. Pat. No. 6,233,482; electroporation may also be used for transfection of cells *in vitro* as described e.g. in US20070128708A1. Electroporation may also be utilized to deliver nucleic acids into cells *in vitro*. Accordingly, electroporation-mediated administration into cells of nucleic acids including expression constructs utilizing any of the many available devices and electroporation systems known to those of skill in the art presents an exciting new means for delivering an RNA of interest to a target cell.

5.7.1.1 Sources of T Cells

[0346] Prior to expansion and genetic modification, a source of T cells is obtained from a subject. The term “subject” is intended to include living organisms in which an immune response can be elicited (e.g., mammals). Examples of subjects include humans, dogs, cats, mice, rats, and transgenic species thereof. Preferably, subjects are human.

[0347] T cells can be obtained from a number of sources, including peripheral blood mononuclear cells, bone marrow, lymph node tissue, cord blood, thymus tissue, tissue from a site of infection, ascites, pleural effusion, spleen tissue, and tumors. In certain embodiments of the present disclosure, any number of T cell lines available in the art, may be used. In certain embodiments of the present disclosure, T cells can be obtained from a unit of blood collected from a subject using any number of techniques known to the skilled artisan, such as Ficoll™ separation. In one preferred embodiment, cells from the circulating blood of an individual are obtained by apheresis. The apheresis product typically contains lymphocytes, including T cells, monocytes, granulocytes, B cells, other nucleated white blood cells, red blood cells, and

platelets. In one embodiment, the cells collected by apheresis may be washed to remove the plasma fraction and to place the cells in an appropriate buffer or media for subsequent processing steps. In one embodiment of the disclosure, the cells are washed with phosphate buffered saline (PBS). In an alternative embodiment, the wash solution lacks calcium and may lack magnesium or may lack many if not all divalent cations. Again, surprisingly, initial activation steps in the absence of calcium lead to magnified activation. As those of ordinary skill in the art would readily appreciate a washing step may be accomplished by methods known to those in the art, such as by using a semi-automated "flow-through" centrifuge (for example, the Cobe 2991 cell processor, the Baxter CytoMate, or the Haemonetics Cell Saver 5) according to the manufacturer's instructions. After washing, the cells may be resuspended in a variety of biocompatible buffers, such as, for example, Ca-free, Mg-free PBS, PlasmaLyte A, or other saline solution with or without buffer. Alternatively, the undesirable components of the apheresis sample may be removed and the cells directly resuspended in culture media.

[0348] In another embodiment, T cells are isolated from peripheral blood lymphocytes by lysing the red blood cells and depleting the monocytes, for example, by centrifugation through a PERCOLL™ gradient or by counterflow centrifugal elutriation. A specific subpopulation of T cells, such as CD3⁺, CD28⁺, CD4⁺, CD8⁺, CD45RA⁺ and CD45RO⁺ T cells, can be further isolated by positive or negative selection techniques. For example, in one embodiment, T cells are isolated by incubation with anti-CD3/anti-CD28 (*i.e.*, 3 x 28)-conjugated beads, such as DYNABEADS® M-450 CD3/CD28 T, for a time period sufficient for positive selection of the desired T cells. In one embodiment, the time period is about 30 minutes. In a further embodiment, the time period ranges from 30 minutes to 36 hours or longer and all integer values there between. In a further embodiment, the time period is at least 1, 2, 3, 4, 5, or 6 hours. In yet another preferred embodiment, the time period is 10 to 24 hours. In one preferred embodiment, the incubation time period is 24 hours. For isolation of T cells from patients with leukemia, use of longer incubation times, such as 24 hours, can increase cell yield. Longer incubation times may be used to isolate T cells in any situation where there are few T cells as compared to other cell types, such in isolating tumor infiltrating lymphocytes (TIL) from tumor tissue or from immunocompromised individuals. Further, use of longer incubation times can increase the efficiency of capture of CD8⁺ T cells. Thus, by simply shortening or, lengthening the time T cells are allowed to bind to the CD3/CD28 beads and/or by increasing or decreasing the ratio of beads to T cells (as described further herein), subpopulations of T cells can be preferentially selected for or against at culture initiation or at other time points during the process. Additionally, by increasing or decreasing the ratio of anti-CD3 and/or anti-CD28 antibodies on the beads or other surface, subpopulations of T cells can be preferentially selected for or against at culture initiation or at other desired time points. The skilled artisan would recognize that multiple rounds of selection can also be used in the context of this disclosure. In certain embodiments, it may be desirable to perform the selection procedure and

use the “unselected” cells in the activation and expansion process. “Unselected” cells can also be subjected to further rounds of selection.

[0349] Enrichment of a T cell population by negative selection can be accomplished with a combination of antibodies directed to surface markers unique to the negatively selected cells. One method is cell sorting and/or selection via negative magnetic immunoadherence or flow cytometry that uses a cocktail of monoclonal antibodies directed to cell surface markers present on the cells negatively selected. For example, to enrich for CD4⁺ cells by negative selection, a monoclonal antibody cocktail typically includes antibodies to CD14, CD20, CD11b, CD16, HLA-DR, and CD8. In certain embodiments, it may be desirable to enrich for or positively select for regulatory T cells which typically express CD4⁺, CD25⁺, CD62L^{hi}, GITR⁺, and FoxP3⁺. Alternatively, in certain embodiments, T regulatory cells are depleted by anti-CD25 conjugated beads or other similar method of selection.

[0350] For isolation of a desired population of cells by positive or negative selection, the concentration of cells and surface (e.g., particles such as beads) can be varied. In certain embodiments, it may be desirable to significantly decrease the volume in which beads and cells are mixed together (i.e., increase the concentration of cells), to ensure maximum contact of cells and beads. For example, in one embodiment, a concentration of 2 billion cells/ml is used. In one embodiment, a concentration of 1 billion cells/ml is used. In a further embodiment, greater than 100 million cells/ml is used. In a further embodiment, a concentration of cells of 10, 15, 20, 25, 30, 35, 40, 45, or 50 million cells/ml is used. In yet another embodiment, a concentration of cells from 75, 80, 85, 90, 95, or 100 million cells/ml is used. In further embodiments, concentrations of 125 or 150 million cells/ml can be used. Using high concentrations can result in increased cell yield, cell activation, and cell expansion. Further, use of high cell concentrations allows more efficient capture of cells that may weakly express target antigens of interest, such as CD28-negative T cells, or from samples where there are many tumor cells present (i.e., leukemic blood, tumor tissue, etc.). Such populations of cells may have therapeutic value and would be desirable to obtain. For example, using high concentration of cells allows more efficient selection of CD8⁺ T cells that normally have weaker CD28 expression.

[0351] In a related embodiment, it may be desirable to use lower concentrations of cells. By significantly diluting the mixture of T cells and surface (e.g., particles such as beads), interactions between the particles and cells are minimized. This selects for cells that express high amounts of desired antigens to be bound to the particles. For example, CD4⁺ T cells express higher levels of CD28 and are more efficiently captured than CD8⁺ T cells in dilute concentrations. In one embodiment, the concentration of cells used is 5×10^6 /ml. In other embodiments, the concentration used can be from about 1×10^5 /ml to 1×10^6 /ml, and any integer value in between.

[0352] In other embodiments, the cells may be incubated on a rotator for varying lengths of time at varying speeds at either 2-10° C. or at room temperature.

[0353] T cells for stimulation can also be frozen after a washing step. Wishing not to be bound by theory, the freeze and subsequent thaw step provides a more uniform product by removing granulocytes and to some extent monocytes in the cell population. After the washing step that removes plasma and platelets, the cells may be suspended in a freezing solution. While many freezing solutions and parameters are known in the art and will be useful in this context, one method involves using PBS containing 20% DMSO and 8% human serum albumin, or culture media containing 10% Dextran 40 and 5% Dextrose, 20% Human Serum Albumin and 7.5% DMSO, or 31.25% Plasmalyte-A, 31.25% Dextrose 5%, 0.45% NaCl, 10% Dextran 40 and 5% Dextrose, 20% Human Serum Albumin, and 7.5% DMSO or other suitable cell freezing media containing for example, Hespan and PlasmaLyte A, the cells then are frozen to -80° C. at a rate of 1° per minute and stored in the vapor phase of a liquid nitrogen storage tank. Other methods of controlled freezing may be used as well as uncontrolled freezing immediately at -20° C. or in liquid nitrogen.

[0354] In certain embodiments, cryopreserved cells are thawed and washed as described herein and allowed to rest for one hour at room temperature prior to activation using the methods of the present disclosure.

[0355] Also contemplated in the context of the disclosure is the collection of blood samples or apheresis product from a subject at a time period prior to when the expanded cells as described herein might be needed. As such, the source of the cells to be expanded can be collected at any time point necessary, and desired cells, such as T cells, isolated and frozen for later use in T cell therapy for any number of diseases or conditions that would benefit from T cell therapy, such as those described herein. In one embodiment a blood sample or an apheresis is taken from a generally healthy subject. In certain embodiments, a blood sample or an apheresis is taken from a generally healthy subject who is at risk of developing a disease, but who has not yet developed a disease, and the cells of interest are isolated and frozen for later use. In certain embodiments, the T cells may be expanded, frozen, and used at a later time. In certain embodiments, samples are collected from a patient shortly after diagnosis of a particular disease as described herein but prior to any treatments. In a further embodiment, the cells are isolated from a blood sample or an apheresis from a subject prior to any number of relevant treatment modalities, including but not limited to treatment with agents such as natalizumab, efalizumab, antiviral agents, chemotherapy, radiation, immunosuppressive agents, such as cyclosporin, azathioprine, methotrexate, mycophenolate, and FK506, antibodies, or other immunoablative agents such as CAMPATH, anti-CD3 antibodies, cytoxan, fludarabine, cyclosporin, FK506, rapamycin, mycophenolic acid, steroids, FR901228, and irradiation. These drugs inhibit either the calcium dependent phosphatase calcineurin (cyclosporine and FK506)

or inhibit the p70S6 kinase that is important for growth factor induced signaling (rapamycin). (Liu *et al.*, Cell 66:807-815, 1991; Henderson *et al.*, Immun. 73:316-321, 1991; Bierer *et al.*, Curr. Opin. Immun. 5:763-773, 1993). In a further embodiment, the cells are isolated for a patient and frozen for later use in conjunction with (e.g., before, simultaneously or following) bone marrow or stem cell transplantation or T cell ablative therapy using either chemotherapy agents such as, fludarabine, external-beam radiation therapy (XRT), cyclophosphamide.

[0356] In a further embodiment of the present disclosure, T cells are obtained from a patient directly following treatment. In this regard, it has been observed that following certain cancer treatments, in particular treatments with drugs that damage the immune system, shortly after treatment during the period when patients would normally be recovering from the treatment, the quality of T cells obtained may be optimal or improved for their ability to expand *ex vivo*. Likewise, following *ex vivo* manipulation using the methods described herein, these cells may be in a preferred state for enhanced engraftment and *in vivo* expansion. Thus, it is contemplated within the context of the present disclosure to collect blood cells, including T cells, dendritic cells, or other cells of the hematopoietic lineage, during this recovery phase. Further, in certain embodiments, mobilization (for example, mobilization with GM-CSF) and conditioning regimens can be used to create a condition in a subject wherein repopulation, recirculation, regeneration, and/or expansion of particular cell types is favored, especially during a defined window of time following therapy. Illustrative cell types include T cells, B cells, dendritic cells, and other cells of the immune system.

5.7.1.2 Activation and Expansion of T Cells

[0357] T cells are activated and expanded generally using methods as described, for example, in U.S. Pat. Nos. 6,352,694; 6,534,055; 6,905,680; 6,692,964; 5,858,358; 6,887,466; 6,905,681; 7,144,575; 7,067,318; 7,172,869; 7,232,566; 7,175,843; 5,883,223; 6,905,874; 6,797,514; 6,867,041; and U.S. Patent Application Publication No. 20060121005.

[0358] Generally, the T cells of the disclosure are expanded by contact with a surface having attached thereto an agent that stimulates a CD3/TCR complex associated signal and a ligand that stimulates a co-stimulatory molecule on the surface of the T cells. In particular, T cell populations may be stimulated as described herein, such as by contact with an anti-CD3 antibody, or antigen-binding fragment thereof, or an anti-CD2 antibody immobilized on a surface, or by contact with a protein kinase C activator (e.g., bryostatin) in conjunction with a calcium ionophore. For co-stimulation of an accessory molecule on the surface of the T cells, a ligand that binds the accessory molecule is used. For example, a population of T cells can be contacted with an anti-CD3 antibody and an anti-CD28 antibody, under conditions appropriate for stimulating proliferation of the T cells. To stimulate proliferation of either CD4⁺ T cells or CD8⁺ T cells, an anti-CD3 antibody and an anti-CD28 antibody. Examples of an anti-CD28 antibody include 9.3, B-T3, XR-CD28 (Diaclone, Besancon, France) can be used as can other

methods commonly known in the art (Berg *et al.*, Transplant Proc. 30(8):3975-3977, 1998; Haanen *et al.*, J. Exp. Med. 190(9):1319-1328, 1999; Garland *et al.*, J. Immunol Meth. 227(1-2):53-63, 1999).

[0359] In certain embodiments, the primary stimulatory signal and the co-stimulatory signal for the T cell may be provided by different protocols. For example, the agents providing each signal may be in solution or coupled to a surface. When coupled to a surface, the agents may be coupled to the same surface (*i.e.*, in "cis" formation) or to separate surfaces (*i.e.*, in "trans" formation). Alternatively, one agent may be coupled to a surface and the other agent in solution. In one embodiment, the agent providing the co-stimulatory signal is bound to a cell surface and the agent providing the primary activation signal is in solution or coupled to a surface. In certain embodiments, both agents can be in solution. In another embodiment, the agents may be in soluble form, and then cross-linked to a surface, such as a cell expressing Fc receptors or an antibody or other binding agent which will bind to the agents. In this regard, see for example, U.S. Patent Application Publication Nos. 20040101519 and 20060034810 for artificial antigen presenting cells (APCs) that are contemplated for use in activating and expanding T cells in the present disclosure.

[0360] In one embodiment, the two agents are immobilized on beads, either on the same bead, *i.e.*, "cis," or to separate beads, *i.e.*, "trans." By way of example, the agent providing the primary activation signal is an anti-CD3 antibody or an antigen-binding fragment thereof and the agent providing the co-stimulatory signal is an anti-CD28 antibody or antigen-binding fragment thereof; and both agents are co-immobilized to the same bead in equivalent molecular amounts. In one embodiment, a 1:1 ratio of each antibody bound to the beads for CD4⁺ T cell expansion and T cell growth is used. In certain aspects of the present disclosure, a ratio of anti CD3:CD28 antibodies bound to the beads is used such that an increase in T cell expansion is observed as compared to the expansion observed using a ratio of 1:1. In one particular embodiment an increase of from about 1 to about 3 fold is observed as compared to the expansion observed using a ratio of 1:1. In one embodiment, the ratio of CD3:CD28 antibody bound to the beads ranges from 100:1 to 1:100 and all integer values there between. In one aspect of the present disclosure, more anti-CD28 antibody is bound to the particles than anti-CD3 antibody, *i.e.*, the ratio of CD3:CD28 is less than one. In certain embodiments of the disclosure, the ratio of anti CD28 antibody to anti CD3 antibody bound to the beads is greater than 2:1. In one particular embodiment, a 1:100 CD3:CD28 ratio of antibody bound to beads is used. In another embodiment, a 1:75 CD3:CD28 ratio of antibody bound to beads is used. In a further embodiment, a 1:50 CD3:CD28 ratio of antibody bound to beads is used. In another embodiment, a 1:30 CD3:CD28 ratio of antibody bound to beads is used. In one preferred embodiment, a 1:10 CD3:CD28 ratio of antibody bound to beads is used. In another

embodiment, a 1:3 CD3:CD28 ratio of antibody bound to the beads is used. In yet another embodiment, a 3:1 CD3:CD28 ratio of antibody bound to the beads is used.

[0361] Ratios of particles to cells from 1:500 to 500:1 and any integer values in between may be used to stimulate T cells or other target cells. As those of ordinary skill in the art can readily appreciate, the ratio of particles to cells may depend on particle size relative to the target cell. For example, small sized beads could only bind a few cells, while larger beads could bind many. In certain embodiments the ratio of cells to particles ranges from 1:100 to 100:1 and any integer values in-between and in further embodiments the ratio comprises 1:9 to 9:1 and any integer values in between, can also be used to stimulate T cells. The ratio of anti-CD3- and anti-CD28-coupled particles to T cells that result in T cell stimulation can vary as noted above, however certain preferred values include 1:100, 1:50, 1:40, 1:30, 1:20, 1:10, 1:9, 1:8, 1:7, 1:6, 1:5, 1:4, 1:3, 1:2, 1:1, 2:1, 3:1, 4:1, 5:1, 6:1, 7:1, 8:1, 9:1, 10:1, and 15:1 with one preferred ratio being at least 1:1 particles per T cell. In one embodiment, a ratio of particles to cells of 1:1 or less is used. In one particular embodiment, a preferred particle: cell ratio is 1:5. In further embodiments, the ratio of particles to cells can be varied depending on the day of stimulation. For example, in one embodiment, the ratio of particles to cells is from 1:1 to 10:1 on the first day and additional particles are added to the cells every day or every other day thereafter for up to 10 days, at final ratios of from 1:1 to 1:10 (based on cell counts on the day of addition). In one particular embodiment, the ratio of particles to cells is 1:1 on the first day of stimulation and adjusted to 1:5 on the third and fifth days of stimulation. In another embodiment, particles are added on a daily or every other day basis to a final ratio of 1:1 on the first day, and 1:5 on the third and fifth days of stimulation. In another embodiment, the ratio of particles to cells is 2:1 on the first day of stimulation and adjusted to 1:10 on the third and fifth days of stimulation. In another embodiment, particles are added on a daily or every other day basis to a final ratio of 1:1 on the first day, and 1:10 on the third and fifth days of stimulation. One of skill in the art will appreciate that a variety of other ratios may be suitable for use in the present disclosure. In particular, ratios will vary depending on particle size and on cell size and type.

[0362] In further embodiments of the present disclosure, the cells, such as T cells, are combined with agent-coated beads, the beads and the cells are subsequently separated, and then the cells are cultured. In an alternative embodiment, prior to culture, the agent-coated beads and cells are not separated but are cultured together. In a further embodiment, the beads and cells are first concentrated by application of a force, such as a magnetic force, resulting in increased ligation of cell surface markers, thereby inducing cell stimulation.

[0363] By way of example, cell surface proteins may be ligated by allowing paramagnetic beads to which anti-CD3 and anti-CD28 are attached (3 x 28 beads) to contact the T cells. In one embodiment the cells (for example, 10^4 to 10^9 T cells) and beads (for example, DYNABEADS® M-450 CD3/CD28 T paramagnetic beads at a ratio of 1:1) are combined in a

buffer, preferably PBS (without divalent cations such as, calcium and magnesium). Again, those of ordinary skill in the art can readily appreciate any cell concentration may be used. For example, the target cell may be very rare in the sample and comprise only 0.01% of the sample or the entire sample (*i.e.*, 100%) may comprise the target cell of interest. Accordingly, any cell number is within the context of the present disclosure. In certain embodiments, it may be desirable to significantly decrease the volume in which particles and cells are mixed together (*i.e.*, increase the concentration of cells), to ensure maximum contact of cells and particles. For example, in one embodiment, a concentration of about 2 billion cells/ml is used. In another embodiment, greater than 100 million cells/ml is used. In a further embodiment, a concentration of cells of 10, 15, 20, 25, 30, 35, 40, 45, or 50 million cells/ml is used. In yet another embodiment, a concentration of cells from 75, 80, 85, 90, 95, or 100 million cells/ml is used. In further embodiments, concentrations of 125 or 150 million cells/ml can be used. Using high concentrations can result in increased cell yield, cell activation, and cell expansion. Further, use of high cell concentrations allows more efficient capture of cells that may weakly express target antigens of interest, such as CD28-negative T cells. Such populations of cells may have therapeutic value and would be desirable to obtain in certain embodiments. For example, using high concentration of cells allows more efficient selection of CD8⁺ T cells that normally have weaker CD28 expression.

[0364] In one embodiment of the present disclosure, the mixture may be cultured for several hours (about 3 hours) to about 14 days or any hourly integer value in between. In another embodiment, the mixture may be cultured for 21 days. In one embodiment of the disclosure the beads and the T cells are cultured together for about eight days. In another embodiment, the beads and T cells are cultured together for 2-3 days. Several cycles of stimulation may also be desired such that culture time of T cells can be 60 days or more. Conditions appropriate for T cell culture include an appropriate media (*e.g.*, Minimal Essential Media or RPMI Media 1640 or, X-vivo 15, (Lonza)) that may contain factors necessary for proliferation and viability, including serum (*e.g.*, fetal bovine or human serum), interleukin-2 (IL-2), insulin, IFN- γ , IL-4, IL-7, GM-CSF, IL-10, IL-12, IL-15, TGF β , and TNF- α or any other additives for the growth of cells known to the skilled artisan. Other additives for the growth of cells include, but are not limited to, surfactant, plasmanate, and reducing agents such as N-acetyl-cysteine and 2-mercaptoethanol. Media can include RPMI 1640, AIM-V, DMEM, MEM, α -MEM, F-12, X-Vivo 15, and X-Vivo 20, Optimizer, with added amino acids, sodium pyruvate, and vitamins, either serum-free or supplemented with an appropriate amount of serum (or plasma) or a defined set of hormones, and/or an amount of cytokine(s) sufficient for the growth and expansion of T cells. Antibiotics, *e.g.*, penicillin and streptomycin, are included only in experimental cultures, not in cultures of cells that are to be infused into a subject. The target cells are maintained under conditions necessary to support growth, for example, an appropriate temperature (*e.g.*, 37° C.) and atmosphere (*e.g.*, air plus 5% CO₂).

[0365] T cells that have been exposed to varied stimulation times may exhibit different characteristics. For example, typical blood or apheresed peripheral blood mononuclear cell products have a helper T cell population (T_H , $CD4^+$) that is greater than the cytotoxic or suppressor T cell population (T_C , $CD8^+$). Ex vivo expansion of T cells by stimulating CD3 and CD28 receptors produces a population of T cells that prior to about days 8-9 consists predominately of T_H cells, while after about days 8-9, the population of T cells comprises an increasingly greater population of T_C cells. Accordingly, depending on the purpose of treatment, infusing a subject with a T cell population comprising predominately of T_H cells may be advantageous. Similarly, if an antigen-specific subset of T_C cells has been isolated it may be beneficial to expand this subset to a greater degree.

[0366] Further, in addition to CD4 and CD8 markers, other phenotypic markers vary significantly, but in large part, reproducibly during the course of the cell expansion process. Thus, such reproducibility enables the ability to tailor an activated T cell product for specific purposes.

5.8 Compositions

[0367] The anti-glyco-LAMP1 antibodies, fusion proteins, and/or anti-glyco-LAMP1 ADCs of the disclosure may be in the form of compositions comprising the anti-glyco-LAMP1 antibody, fusion protein and/or ADC and one or more carriers, excipients and/or diluents. The compositions may be formulated for specific uses, such as for veterinary uses or pharmaceutical uses in humans. The form of the composition (*e.g.*, dry powder, liquid formulation, *etc.*) and the excipients, diluents and/or carriers used will depend upon the intended uses of the antibody, fusion protein and/or ADC and, for therapeutic uses, the mode of administration.

[0368] For therapeutic uses, the compositions may be supplied as part of a sterile, pharmaceutical composition that includes a pharmaceutically acceptable carrier. This composition can be in any suitable form (depending upon the desired method of administering it to a patient). The pharmaceutical composition can be administered to a patient by a variety of routes such as orally, transdermally, subcutaneously, intranasally, intravenously, intramuscularly, intratumorally, intrathecally, topically or locally. The most suitable route for administration in any given case will depend on the particular antibody and/or ADC, the subject, and the nature and severity of the disease and the physical condition of the subject. Typically, the pharmaceutical composition will be administered intravenously or subcutaneously.

[0369] Pharmaceutical compositions can be conveniently presented in unit dosage forms containing a predetermined amount of an anti-glyco-LAMP1 antibody and/or anti-glyco-LAMP1 ADC of the disclosure per dose. The quantity of antibody and/or ADC included in a unit dose will depend on the disease being treated, as well as other factors as are well known in the art. Such unit dosages may be in the form of a lyophilized dry powder containing an amount of

antibody and/or ADC suitable for a single administration, or in the form of a liquid. Dry powder unit dosage forms may be packaged in a kit with a syringe, a suitable quantity of diluent and/or other components useful for administration. Unit dosages in liquid form may be conveniently supplied in the form of a syringe pre-filled with a quantity of antibody and/or ADC suitable for a single administration.

[0370] The pharmaceutical compositions may also be supplied in bulk from containing quantities of ADC suitable for multiple administrations.

[0371] Pharmaceutical compositions may be prepared for storage as lyophilized formulations or aqueous solutions by mixing an antibody, fusion protein, and/or ADC having the desired degree of purity with optional pharmaceutically acceptable carriers, excipients or stabilizers typically employed in the art (all of which are referred to herein as "carriers"), *i.e.*, buffering agents, stabilizing agents, preservatives, isotonicifiers, non-ionic detergents, antioxidants, and other miscellaneous additives. See, Remington's Pharmaceutical Sciences, 16th edition (Osol, ed. 1980). Such additives should be nontoxic to the recipients at the dosages and concentrations employed.

[0372] Buffering agents help to maintain the pH in the range which approximates physiological conditions. They may be present at a wide variety of concentrations, but will typically be present in concentrations ranging from about 2 mM to about 50 mM. Suitable buffering agents for use with the present disclosure include both organic and inorganic acids and salts thereof such as citrate buffers (*e.g.*, monosodium citrate-disodium citrate mixture, citric acid-trisodium citrate mixture, citric acid-monosodium citrate mixture, *etc.*), succinate buffers (*e.g.*, succinic acid-monosodium succinate mixture, succinic acid-sodium hydroxide mixture, succinic acid-disodium succinate mixture, *etc.*), tartrate buffers (*e.g.*, tartaric acid-sodium tartrate mixture, tartaric acid-potassium tartrate mixture, tartaric acid-sodium hydroxide mixture, *etc.*), fumarate buffers (*e.g.*, fumaric acid-monosodium fumarate mixture, fumaric acid-disodium fumarate mixture, monosodium fumarate-disodium fumarate mixture, *etc.*), gluconate buffers (*e.g.*, gluconic acid-sodium glyconate mixture, gluconic acid-sodium hydroxide mixture, gluconic acid-potassium glyconate mixture, *etc.*), oxalate buffer (*e.g.*, oxalic acid-sodium oxalate mixture, oxalic acid-sodium hydroxide mixture, oxalic acid-potassium oxalate mixture, *etc.*), lactate buffers (*e.g.*, lactic acid-sodium lactate mixture, lactic acid-sodium hydroxide mixture, lactic acid-potassium lactate mixture, *etc.*) and acetate buffers (*e.g.*, acetic acid-sodium acetate mixture, acetic acid-sodium hydroxide mixture, *etc.*). Additionally, phosphate buffers, histidine buffers and trimethylamine salts such as Tris can be used.

[0373] Preservatives may be added to retard microbial growth, and can be added in amounts ranging from about 0.2%-1% (w/v). Suitable preservatives for use with the present disclosure include phenol, benzyl alcohol, meta-cresol, methyl paraben, propyl paraben, octadecyldimethylbenzyl ammonium chloride, benzalconium halides (*e.g.*, chloride, bromide,

and iodide), hexamethonium chloride, and alkyl parabens such as methyl or propyl paraben, catechol, resorcinol, cyclohexanol, and 3-pentanol. Isotonicifiers sometimes known as "stabilizers" can be added to ensure isotonicity of liquid compositions of the present disclosure and include polyhydric sugar alcohols, for example trihydric or higher sugar alcohols, such as glycerin, erythritol, arabitol, xylitol, sorbitol and mannitol. Stabilizers refer to a broad category of excipients which can range in function from a bulking agent to an additive which solubilizes the therapeutic agent or helps to prevent denaturation or adherence to the container wall. Typical stabilizers can be polyhydric sugar alcohols (enumerated above); amino acids such as arginine, lysine, glycine, glutamine, asparagine, histidine, alanine, ornithine, L-leucine, 2-phenylalanine, glutamic acid, threonine, *etc.*, organic sugars or sugar alcohols, such as lactose, trehalose, stachyose, mannitol, sorbitol, xylitol, ribitol, myoinositol, galactitol, glycerol and the like, including cyclitols such as inositol; polyethylene glycol; amino acid polymers; sulfur containing reducing agents, such as urea, glutathione, thiocetic acid, sodium thioglycolate, thioglycerol, α -monothioglycerol and sodium thio sulfate; low molecular weight polypeptides (*e.g.*, peptides of 10 residues or fewer); proteins such as human serum albumin, bovine serum albumin, gelatin or immunoglobulins; hydrophylic polymers, such as polyvinylpyrrolidone monosaccharides, such as xylose, mannose, fructose, glucose; disaccharides such as lactose, maltose, sucrose and trehalose; and trisaccharides such as raffinose; and polysaccharides such as dextran. Stabilizers may be present in amounts ranging from 0.5 to 10 wt % per wt of ADC.

[0374] Non-ionic surfactants or detergents (also known as "wetting agents") may be added to help solubilize the glycoprotein as well as to protect the glycoprotein against agitation-induced aggregation, which also permits the formulation to be exposed to shear surface stressed without causing denaturation of the protein. Suitable non-ionic surfactants include polysorbates (20, 80, *etc.*), polyoxamers (184, 188 *etc.*), and pluronic polyols. Non-ionic surfactants may be present in a range of about 0.05 mg/mL to about 1.0 mg/mL, for example about 0.07 mg/mL to about 0.2 mg/mL.

[0375] Additional miscellaneous excipients include bulking agents (*e.g.*, starch), chelating agents (*e.g.*, EDTA), antioxidants (*e.g.*, ascorbic acid, methionine, vitamin E), and cosolvents.

5.9 Methods of Use

[0376] The anti-glyco-LAMP1 antibody or binding fragments described herein can be used in various diagnostic and therapeutic methods. In some embodiments, a patient can be diagnosed with a cancer using any method as described herein (*e.g.*, as described in Section 5.9.1) and subsequently treated using any method as described herein (*e.g.*, as described in Section 5.9.2). The diagnostic methods described herein (*e.g.*, as described in Section 5.9.1) can be utilized to monitor the patient's cancer status during or following cancer therapy (including but not limited to cancer therapy as described in Section 5.9.2).

5.9.1. Diagnostic Methods

[0377] The anti-glyco-LAMP1 antibody or binding fragments (including immunoconjugates and labeled antibodies and binding fragments) can be used in diagnostic assays. For example, the antibodies and binding fragments can be employed in immunoassays, such as competitive binding assays, direct and indirect sandwich assays, and immunoprecipitation assays, including immunohistochemistry, enzyme-linked immunosorbent assay (ELISA), fluorescence-activated cell sorting (FACS), and Western blots.

[0378] The anti-glyco-LAMP1 antibody or binding fragments described herein can be used in a detection assay and/or a diagnostic assay to detect a biomarker in a sample, such as, *e.g.*, a patient-derived biological sample. The biomarker may be a protein biomarker (*e.g.*, a tumor-associated glycoform of LAMP-1, for example a glycoform of LAMP-1 comprising the amino acid sequence CEQDRPSP**T**APPAPPSPSP (SEQ ID NO:200) and glycosylated with GalNAc on the threonine residue shown in bold underlined text) present on the surface of or within, *e.g.*, a cancer cell or a cancer-derived extracellular vesicle.

[0379] An anti-glyco-LAMP1 antibody or antigen-binding fragment of the disclosure can be used in a method of detecting a biomarker in a sample comprising one or more EVs (*e.g.*, a liquid biopsy). In such embodiments, an EV surface biomarker is recognized by the anti-glyco-LAMP1 antibody or antigen-binding fragment of the disclosure. Exemplary methods of detecting the biomarker include, but are not limited to, capture assays, immunoassays, such as immunoprecipitation; Western blot; ELISA; immunohistochemistry; immunocytochemistry; flow cytometry; and immuno-PCR. In some embodiments, an immunoassay can be a chemiluminescent immunoassay. In some embodiments, an immunoassay can be a high-throughput and/or automated immunoassay platform.

[0380] The anti-glyco-LAMP1 antibody or binding fragments described herein also are useful for radiographic *in vivo* imaging, wherein an antibody labeled with a detectable moiety such as a radio-opaque agent or radioisotope is administered to a subject, preferably into the bloodstream, and the presence and location of the labeled antibody in the host is assayed. This imaging technique is useful in the staging and treatment of malignancies.

5.9.2. Therapeutic Methods

[0381] The anti-glyco-LAMP1 antibody or binding fragments, fusion proteins, ADCs and CARs, and chimeric TCRs described herein are useful for treatment of glyco-LAMP1 expressing cancers, including colorectal neoplasm, colon adenocarcinoma, pancreatic adenocarcinoma, breast adenocarcinoma, and Non-Small Cell Lung Cancer.

[0382] Thus, the disclosure provides anti-glyco-LAMP1 antibodies, binding fragments, fusion proteins, ADCs, CARs, and chimeric TCRs as described herein for use as a medicament, for example for use in the treatment of cancer, *e.g.*, any of the cancers identified in the previous paragraph, for use in a diagnostic assay, and for use in radiographic *in vivo* imaging. The

disclosure further provides for the use of the anti-glyco-LAMP1 antibodies, binding fragments, fusion proteins, ADCs, CARs and chimeric TCRs as described herein in the manufacture of a medicament, for example for the treatment of cancer, e.g., any of the cancers identified in the previous paragraph.

[0383] When using the CARs or chimeric TCRs of the disclosure for therapy, the therapeutic methods of the disclosure comprise administering to a subject with a glyco-LAMP1-expressing tumor an effective amount of a genetically modified cell engineered to express a CAR or chimeric TCR of the disclosure, for example a CAR as described in Section 5.3 or in numbered embodiments 558 to 591, a chimeric TCR as described in Section 5.4 or in numbered embodiments 602 to 695, or a MicAbody as described in Section 5.6 and numbered embodiments 539 to 542. Methods of modifying cells, particularly T cells, to express a CAR or chimeric TCR are described in Section 5.7.1.

[0384] When using the MicAbodies of the disclosure for therapy, the therapeutic methods of the disclosure comprise administering to a subject with a glyco-LAMP1-expressing tumor therapeutically effective amounts of a MicAbody of the disclosure, for example a MicAbody described in Section 5.6, and a genetically modified T-cell engineered to express a CAR comprising a NKG2D receptor capable of specifically binding the MicAbody.

5.10 LAMP1 Peptides

[0385] Also provided are isolated LAMP1 glycopeptides, or glyco-LAMP1 peptides, comprising the amino acid CEQDRPSPTTAPPAPPSPSP (SEQ ID NO:155), or a fragment thereof. In some embodiments, the LAMP1 glycopeptide is glycosylated with O-linked GalNAc on (i) the threonine residue at amino acid position 9 of CEQDRPSPTTAPPAPPSPSP (SEQ ID NO:155), (ii) the threonine residues at amino acid positions 9 and 10 of CEQDRPSPTTAPPAPPSPSP (SEQ ID NO:155), (iii) the serine residue at amino acid position 7 and the threonine residue at amino acid 9 of CEQDRPSPTTAPPAPPSPSP (SEQ ID NO:155), or (iv), the serine residue at amino acid position 7 and the threonine residues at amino acid positions 9 and 10 of CEQDRPSPTTAPPAPPSPSP (SEQ ID NO:155).

[0386] In some embodiments the LAMP1 glycopeptide comprises (i) the amino acid CEQDRPSPT**TT**APPAPPSPSP (SEQ ID NO:200), glycosylated with GalNAc on the threonine residue shown in bold and underlined text; (ii) the amino acid CEQDRPSPT**TT**APPAPPSPSP (SEQ ID NO:216), glycosylated with GalNAc on the serine and threonine residues shown in bold and underlined text; (iii) the amino acid CEQDRPS**PT****TT**APPAPPSPSP (SEQ ID NO:217), glycosylated with GalNAc on the serine and threonine residues shown in bold and underlined text; (iv) the amino acid CEQDRPS**PT****TT**APPAPPSPSP (SEQ ID NO:154), glycosylated with GalNAc on the serine and threonine residues shown in bold and underlined text, or (v) a fragment of any one of (i)-(iv). Exemplary isolated LAMP1 glycopeptides and uses thereof are described in numbered embodiments 739 to 771.

[0387] The present disclosure encompasses synthetic synthesis of the isolated LAMP1 glycoproteins and recombinant methods for producing the isolated LAMP1 glycoproteins.

[0388] In certain embodiments, the isolated LAMP1 peptides are synthesized using a solid-phase peptide synthesis (SPPS) strategy. SPPS methods are known in the art. SPPS provides for the rapid assembly of a polypeptide through successive reactions of amino acid derivatives on a solid support. Through repeated cycles of alternating N-terminal deprotection and coupling reactions, successive amino acid derivatives are added to the polypeptide. In other embodiments, isolated LAMP1 peptides are synthesized using a solution-phase peptide synthesis strategy. Solution-phase peptide synthesis methods are known in the art.

[0389] To ensure proper O-linked glycosylation with GalNAc on, e.g., the serine at amino acid position 7 of SEQ ID NO:154 and the threonines at amino acid positions 9 and 10 of SEQ ID NO: 154, pre-synthesized glycosylated amino acids can be used in the elongation reactions.

[0390] Nucleic acid molecules encoding the isolated LAMP1 glycopeptides, vectors comprising such nucleic acids, and host cells capable of producing the isolated LAMP1 glycopeptides of the disclosure are provided. In certain aspects, the nucleic acid molecules encode, and the host cells are capable of expressing, the LAMP1 glycopeptide as well as fusion proteins that include the LAMP1 glycoproteins.

[0391] An isolated LAMP1 glycopeptide of the disclosure can be prepared by recombinant expression in a host cell. To express a LAMP1 glycopeptide recombinantly, a host cell is transfected with a recombinant expression vector carrying DNA encoding the glycopeptide such that the glycopeptide is expressed in the host cell and, optionally, secreted into the medium in which the host cells are cultured, from which medium the glycoproteins can be recovered (*i.e.*, isolated). Standard recombinant DNA methodologies are used to obtain a LAMP1 glycoprotein gene, incorporate the gene into recombinant expression vectors and introduce the vectors into host cells, such as those described in Molecular Cloning; A Laboratory Manual, Second Edition (Sambrook, Fritsch and Maniatis (eds), Cold Spring Harbor, N. Y., 1989), 122 Current Protocols in Molecular Biology (Ausubel, F. M. *et al.*, eds., Greene Publishing Associates, 1989) and in U.S. Pat. No. 4,816,397.

[0392] It is possible to express the LAMP1 glycoproteins of the disclosure in either prokaryotic or eukaryotic host cells. In certain embodiments, expression of LAMP1 glycoprotein is performed in eukaryotic cells, e.g., mammalian host cells. To produce the isolated LAMP1 glycoproteins of the disclosure, a host cell is selected based on its ability to glycosylate, e.g., the serine at amino acid position 7 of SEQ ID NO:154 and the threonines at amino acid positions 9 and 10 of SEQ ID NO:154. An exemplary host cell is the COSMC HEK293 cell.

5.10.1. LAMP1 Peptide Compositions

[0393] The LAMP1 glycopeptides of the disclosure may be in the form of compositions comprising the LAMP1 glycopeptide and one or more carriers, excipients, diluents and/or adjuvants. The compositions may be formulated for specific uses, such as for veterinary uses or pharmaceutical uses in humans. The form of the composition (e.g., dry powder, liquid formulation, etc.) and the excipients, diluents and/or carriers used will depend upon the intended uses of the LAMP1 glycopeptide and, for therapeutic uses, the mode of administration.

[0394] For therapeutic uses, the compositions may be supplied as part of a sterile, pharmaceutical composition that includes a pharmaceutically acceptable carrier and/or a pharmaceutically acceptable adjuvant. This composition can be in any suitable form (depending upon the desired method of administering it to a patient). The pharmaceutical composition can be administered to a patient by a variety of routes such as orally, transdermally, subcutaneously, intranasally, intravenously, intramuscularly, intratumorally, intrathecally, topically or locally. The most suitable route for administration in any given case will depend on the particular LAMP1 glycopeptide to be administered, the subject, and the nature and severity of the disease and the physical condition of the subject. Typically, the pharmaceutical composition will be administered intravenously or subcutaneously.

[0395] Pharmaceutical compositions can be conveniently presented in unit dosage forms containing a predetermined amount of an LAMP1 glycopeptide of the disclosure per dose. The quantity of LAMP1 glycopeptide included in a unit dose will depend on the disease being treated, as well as other factors as are well known in the art. Such unit dosages may be in the form of a lyophilized dry powder containing an amount of LAMP1 glycopeptide suitable for a single administration, or in the form of a liquid. Dry powder unit dosage forms may be packaged in a kit with a syringe, a suitable quantity of diluent and/or other components useful for administration. Unit dosages in liquid form may be conveniently supplied in the form of a syringe pre-filled with a quantity of LAMP1 glycopeptide suitable for a single administration.

[0396] The pharmaceutical compositions may also be supplied in bulk form containing quantities of LAMP1 glycopeptide suitable for multiple administrations.

[0397] Pharmaceutical compositions may be prepared for storage as lyophilized formulations or aqueous solutions by mixing a LAMP1 glycopeptide having the desired degree of purity with optional pharmaceutically acceptable carriers, excipients, adjuvants or stabilizers typically employed in the art (all of which are referred to herein as "carriers"), *i.e.*, buffering agents, stabilizing agents, preservatives, isotonicifiers, non-ionic detergents, antioxidants, and other miscellaneous additives. See, Remington's Pharmaceutical Sciences, 16th edition (Osol, ed. 1980). Such additives should be nontoxic to the recipients at the dosages and concentrations employed.

[0398] In some embodiments, the composition includes one or more pharmaceutically acceptable adjuvants. Adjuvants include, for example, aluminum salts (e.g., amorphous aluminum hydroxyphosphate sulfate (AAHS), aluminum hydroxide, aluminum phosphate, potassium aluminum sulfate (Alum)), dsRNA analogues, lipid A analogues, flagellin, imidazoquinolines, CpG ODN, saponins (e.g., QS21), C-type lectin ligands (e.g., TDB), CD1d ligands (α-galactosylceramide), M F59, AS01, AS02, AS03, AS04, AS15, AF03, GLA-SE, IC31, CAF01, and virosomes. Other adjuvants known in the art, including chemical adjuvants, genetic adjuvants, protein adjuvants, and lipid adjuvants, can also be included in the compositions.

[0399] Buffering agents help to maintain the pH in the range which approximates physiological conditions. They may be present at a wide variety of concentrations, but will typically be present in concentrations ranging from about 2 mM to about 50 mM. Suitable buffering agents for use with the present disclosure include both organic and inorganic acids and salts thereof such as citrate buffers (e.g., monosodium citrate-disodium citrate mixture, citric acid-trisodium citrate mixture, citric acid-monosodium citrate mixture, etc.), succinate buffers (e.g., succinic acid-monosodium succinate mixture, succinic acid-sodium hydroxide mixture, succinic acid-disodium succinate mixture, etc.), tartrate buffers (e.g., tartaric acid-sodium tartrate mixture, tartaric acid-potassium tartrate mixture, tartaric acid-sodium hydroxide mixture, etc.), fumarate buffers (e.g., fumaric acid-monosodium fumarate mixture, fumaric acid-disodium fumarate mixture, monosodium fumarate-disodium fumarate mixture, etc.), gluconate buffers (e.g., gluconic acid-sodium glyconate mixture, gluconic acid-sodium hydroxide mixture, gluconic acid-potassium glyconate mixture, etc.), oxalate buffer (e.g., oxalic acid-sodium oxalate mixture, oxalic acid-sodium hydroxide mixture, oxalic acid-potassium oxalate mixture, etc.), lactate buffers (e.g., lactic acid-sodium lactate mixture, lactic acid-sodium hydroxide mixture, lactic acid-potassium lactate mixture, etc.) and acetate buffers (e.g., acetic acid-sodium acetate mixture, acetic acid-sodium hydroxide mixture, etc.). Additionally, phosphate buffers, histidine buffers and trimethylamine salts such as Tris can be used.

[0400] Preservatives may be added to retard microbial growth, and can be added in amounts ranging from about 0.2%-1% (w/v). Suitable preservatives for use with the present disclosure include phenol, benzyl alcohol, meta-cresol, methyl paraben, propyl paraben, octadecyldimethylbenzyl ammonium chloride, benzalconium halides (e.g., chloride, bromide, and iodide), hexamethonium chloride, and alkyl parabens such as methyl or propyl paraben, catechol, resorcinol, cyclohexanol, and 3-pentanol. Isotonicifiers sometimes known as "stabilizers" can be added to ensure isotonicity of liquid compositions of the present disclosure and include polyhydric sugar alcohols, for example trihydric or higher sugar alcohols, such as glycerin, erythritol, arabitol, xylitol, sorbitol and mannitol. Stabilizers refer to a broad category of excipients which can range in function from a bulking agent to an additive which solubilizes the therapeutic agent or helps to prevent denaturation or adherence to the container wall. Typical

stabilizers can be polyhydric sugar alcohols (enumerated above); amino acids such as arginine, lysine, glycine, glutamine, asparagine, histidine, alanine, ornithine, L-leucine, 2-phenylalanine, glutamic acid, threonine, etc., organic sugars or sugar alcohols, such as lactose, trehalose, stachyose, mannitol, sorbitol, xylitol, ribitol, myoinositol, galactitol, glycerol and the like, including cyclitols such as inositol; polyethylene glycol; amino acid polymers; sulfur containing reducing agents, such as urea, glutathione, thiocetic acid, sodium thioglycolate, thioglycerol, α -monothioglycerol and sodium thio sulfate; low molecular weight polypeptides (e.g., peptides of 10 residues or fewer); proteins such as human serum albumin, bovine serum albumin, gelatin or immunoglobulins; hydrophilic polymers, such as polyvinylpyrrolidone monosaccharides, such as xylose, mannose, fructose, glucose; disaccharides such as lactose, maltose, sucrose and trehalose; and trisaccharides such as raffinose; and polysaccharides such as dextran. Stabilizers may be present in amounts ranging from 0.5 to 10 wt % per wt of LAMP1 peptide.

[0401] Non-ionic surfactants or detergents (also known as "wetting agents") may be added to help solubilize the glycoprotein as well as to protect the glycoprotein against agitation-induced aggregation, which also permits the formulation to be exposed to shear surface stressed without causing denaturation of the protein. Suitable non-ionic surfactants include polysorbates (20, 80, etc.), poloxamers (184, 188 etc.), and pluronic polyols. Non-ionic surfactants may be present in a range of about 0.05 mg/mL to about 1.0 mg/mL, for example about 0.07 mg/mL to about 0.2 mg/mL.

[0402] Additional miscellaneous excipients include bulking agents (e.g., starch), chelating agents (e.g., EDTA), antioxidants (e.g., ascorbic acid, methionine, vitamin E), and cosolvents.

[0403] Exemplary LAMP1 peptide compositions of the disclosure are described in numbered embodiments 766 and 767.

5.10.2. Methods of Using LAMP1 Peptides

[0404] The LAMP1 peptides described herein can be used in the production of antibodies against a tumor-associated form of LAMP1. The LAMP1 peptide can be administered to an animal. The amount of peptide administered can be effective to cause the animal to produce antibodies against the peptide. As used herein, "animal" refers to multicellular eukaryotic organism from the biological kingdom Animalia. In some embodiments, the animal is a mammal. In some embodiments, the animal is a mouse or a rabbit. Resulting antibodies can then be collected from the animal. The LAMP1 peptide can be administered as purified peptide or as part of a composition provided herein.

[0405] The LAMP1 peptides described herein can be used to elicit an immune response against a tumor-associated form of LAMP1. The LAMP1 peptide can be administered to an animal in an amount effective to cause the animal to mount an immune response (e.g., produce antibodies) against the peptide.

[0406] Exemplary methods for using the LAMP1 peptides of the disclosure are described in numbered embodiments 768 to 771.

6. EXAMPLES

6.1 Example 1: Identification and Characterization Of Anti-Glyco-LAMP1 Antibodies

6.1.1. Overview

[0407] Glycans are essential membrane components and neoplastic transformation of human cells is virtually always associated with aberrant glycosylation of proteins and lipids. There are several types of protein glycosylation, including N-glycosylation and many types of O-glycosylation, but one of the most diverse types is the mucin type GalNAc type O-glycosylation (hereafter called O-glycosylation). Cancer associated changes in O-glycans are particularly interesting and the most frequently observed aberrant glycophenotype is expression of the most immature truncated O-glycan structures designated Tn (GalNAc α 1-O-Ser/Thr), STn (NeuAc α 2-6GalNAc α 1-O-Ser/Thr), and T (Gal β 1-3GalNAc α 1-O-Ser/Thr) antigens. Truncated O-glycans are observed on almost all epithelial cancer cells and strongly correlated with poor prognosis. In addition, it is becoming increasingly clear that glycans also have pivotal roles in cancer development, with truncated O-glycans affecting differentiation, cell-cell and cell-matrix interactions, directly inducing oncogenic features in predisposed cells.

[0408] The inventors have identified LAMP1 glycopeptide epitopes in human cancer cells and used the defined glyco-peptides to develop cancer specific anti-glyco-LAMP1 monoclonal antibodies.

6.1.2. Materials and Methods

6.1.2.1 Synthesis of Tn LAMP1 glycopeptide

[0409] The LAMP1 glycopeptide, CEQDRPSPTTAPPAPPSPSP (SEQ ID NO:154), with O-linked GalNAc on the serine and threonine residues shown with bold and underlined text was synthesized using a standard Fmoc peptide synthesis strategy. Pre-synthesized glycosylated amino acids were coupled to the elongating peptide at specific locations using solid or solution phase peptide chemistry in a stepwise fashion. After completing the full sequence and removing all protecting groups, the resulting glycopeptide was purified by high-performance liquid chromatography (HPLC) and characterized by mass spectrometry (electrospray ionization in positive mode).

6.1.2.1 Synthesis of recombinant Tn-glycosylated LAMP1

[0410] 1×10^6 COSMC KO HEK293 cells in 30mL Opti-MEM were transfected using 30 μ g of a plasmid encoding his-tagged human LAMP1 and 60 μ L 293fectin™ Transfection Reagent (Gibco). Following 48 hours of culture, the cells were spun down and the his-tagged recombinant LAMP1 protein was purified from the supernatant using a 50% Ni-NTA agarose

slurry column (Invitrogen), eluting with 250mM imidazole. To increase purity, this purification step was repeated. The recombinant SC-LAMP1 protein was concentrated in PBS using Amicon Ultra centrifugal filters.

6.1.2.2 Immunization Protocol

[0411] Female Balb/c mice were immunized subcutaneously with the Tn-glycosylated LAMP1 glycopeptide conjugated to KLH (keyhole limpet hemocyanin) through a maleimide linker. The mice were immunized on days 0, 14, and 35 with 50 µg, 45 µg, and 45 µg of KLH-glycopeptide, respectively. The first immunization used Freund's complete adjuvant. All subsequent immunizations used Freund's incomplete adjuvant. On Day 45, tail bleeds were evaluated for polyclonal response. On day 56 or after, mice to be fused were boosted with 15 µg of KLH-glycopeptide in Freund's incomplete adjuvant 3 to 5 days before hybridoma fusion. Splenocytes from mice were fused with SP2/0-Ag14 (ATCC, cat# CRL-1581) myeloma cells using the Electro Cell Manipulator (ECM2001) from BTX Harvard Apparatus. Hybridomas were seeded in 96-well plates, cultured, scaled, and evaluated and selected for specificity towards LAMP1-Tn using ELISA, FLOW cytometry, and immunofluorescence to obtain monoclonal antibodies having specificity for LAMP1-Tn.

6.1.2.3 ELISA

[0412] 96-well Corning high bind microplates (Fisher) were coated overnight at 4 °C with various concentrations of protein, peptide, or glycopeptide in 0.2 M bicarbonate-carbonate buffer (pH 9.4). The plates were then blocked for 1 hour at room temperature with Phosphate-buffered saline (PBS) (pH 7.4) containing 2.5% BSA. Contents of the plate were discarded and purified antibody, or hybridoma supernatants, or blood serum for polyclonal responses, were added at various concentrations and incubated for two hours at room temperature. Plates were washed with tris-buffered saline with 0.05% Tween-20 and then incubated for 1 hour at room temperature with a 1:3000 dilution of HRP conjugated goat anti-mouse IgG Fcγ (Sigma). The plates were washed again and developed with TMB chromogen substrate. After proper development (approximately 2-3 min), the reaction was stopped with 0.2 N H₂SO₄ and the absorbance was read at 450 nm. Data was analysed in GraphPad Prism Software.

6.1.2.4 Flow Cytometry

[0413] Adherent cells were dissociated with TrypLE select (Gibco) and washed from flask surface with cell culture media (RPMI w/ L-glutamine, 1% PenStrep, & 10% FBS). Cells were washed several times by centrifugation at 300*g for 5 min at 4 °C followed by resuspension in PBS with 1% BSA (PBS/1%BSA). Cells were resuspended between 5x10⁵ cells/ml to 2x10⁶ cell/ml and then distributed into a 96 well U-bottom plate. Diluted commercial antibody (0.25-2 µg/ml), or hybridoma supernatants, or blood serum for polyclonal responses, were added to cells and incubated for 1 hr on ice. Following several washes with PBS/1% BSA, cells were incubated for 30 min on ice with a 1:1600 dilution of AlexaFluor647 conjugated F(ab)₂ goat anti-

mouse IgG Fc γ (JacksonImmunoResearch). Cells were washed again with PBS/1% BSA and then fixed in 1% formaldehyde in PBS/1% BSA. Cells were analysed on either a 2 or 4 laser Attune NXT flow cytometer. Data was processed in FlowJo Software.

6.1.2.5 Immunofluorescence

[0414] Cells were seeded to 50% confluency in glass chamber slides (Nunc) and incubated 12-18 hours at 37 °C 5% CO₂. Following overnight growth, media from slides was removed and cells were fixed with 4% formaldehyde in PBS (pH 7.4) for 10 min at room temperature. Slides were washed in PBS. Diluted commercial antibody (1-4 ug/ml), or hybridoma supernatants, or blood serum for polyclonal responses, were added to the slides and the slides were incubated overnight at 4 °C. The slides were washed in PBS and stained with a 1:800 dilution of AlexaFluor488 conjugated F(ab)₂ rabbit anti-mouse IgG (H+L) (Invitrogen) for 45 min at room temperature. The slides were washed in PBS and mounted using Prolong Gold Antifade Mountant with DAPI (Thermofisher) and examined using an Olympus FV3000 confocal microscope.

6.2 Example 2: Functional characterization of 3C7.2C11.1C9, 13C3.1C8.1C9, and 13G2.1A10.2G5 antibodies by Octet and Biacore

6.2.1. Overview

[0415] 3C7.2C11.1C9 (hereinafter, “3C7”), 13C3.1C8.1C9 (hereinafter, “13C3”), and 13G2.1A10.2G5 (hereinafter “13G2”) were characterized by Biacore to test the reactivity of anti-LAMP1 mAbs to titrated LAMP1 peptides. 3C7, 13C3, and 13G2 were also characterized by Octet to test the reactivity of anti-LAMP1 mAbs to peptides with different glycosylated sites (including a non-glycosylated peptide) as shown in Table 6.

Table 6	
Peptide	Sequence (Bold and Underlined= GaINAc Site)
LAMP1-Tn	Biotin-CEQDRP <u>SPTT</u> APPAPPSPSP (SEQ ID NO:154)
LAMP1-Tn (S)	Biotin-CEQDRP <u>SPTT</u> APPAPPSPSP (SEQ ID NO:199)
LAMP1-Tn (T1)	Biotin-CEQDRPSPT <u>T</u> APPAPPSPSP (SEQ ID NO:200)
LAMP1-Tn (T2)	Biotin-CEQDRPSPT <u>T</u> APPAPPSPSP (SEQ ID NO:201)
LAMP1	Biotin-CEQDRPSPTTAPPAPPSPSP (SEQ ID NO:155)

6.2.2. Materials and Methods

6.2.2.1 Surface Plasmon Resonance

[0416] Antibody affinity assays can be carried out using surface plasmon resonance (e.g., using a Biacore system (Cytiva)). In a surface plasmon resonance assay, one or more antibodies can be immobilized onto a biosensor and presented with an analyte (e.g., the LAMP1-Tn peptide Biotin-CEQDRP**SPTT**APPAPPSPSP (the amino acid portion of which is

SEQ ID NO: 154; bold and underlined residues indicate GalNAc glycosylation sites) or a negative control analyte such as an unglycosylated LAMP1 peptide (Biotin-CEQDRPSPTTAPPAPPSPSP (the amino acid portion of which is SEQ ID NO: 155)). The antibodies are contacted with different concentrations of the analyte, for example concentrations of 2.5 nM, 7.4 nM, 22 nM, 66 nM and 200 nM. Affinity is measured using multi-cycle kinetics in triplicate for each analyte concentration, with 1 min association and 5 min dissociation. When comparing the binding affinities of two antibodies, the same concentration of both antibodies was used (e.g., measured using a 1 μ M concentration of each antibody). The affinity is determined by fitting the binding curve to a specific model: kinetic fit (1:1 model) or if applicable heterogeneous ligand binding model.

6.2.2.2 Bio-Layer Interferometry (Octet)

[0417] Antibody affinity and epitope binning of monoclonal antibodies can be assessed against specific antigens using BLI. In a BLI assay, the antigen can be immobilized onto a biosensor (e.g., the LAMP1-Tn peptide Biotin-CEQDRP**SPTT**APPAPPSPSP (the amino acid portion of which is SEQ ID NO: 154) or a negative control analyte such as an unglycosylated LAMP1 peptide (Biotin-CEQDRPSPTTAPPAPPSPSP (the amino acid portion of which is SEQ ID NO: 155)) and presented to one antibody for affinity measurements or two competing antibodies in tandem (or consecutive steps) for epitope binning. The binding to non-overlapping epitopes occurs if saturation with the first antibody does not block the binding of the second antibody. The affinity is determined by fitting the binding curve to a specific model: a 1:1 monovalent model or a 2:1 bivalent model. The error (>95% confidence) is calculated by how close the generated curve matches the model.

6.2.2.3 Flow Cytometry

[0418] Adherent cells were dissociated with TrypLE select (Gibco) and washed from the flask surface with cell culture media (RPMI w/ L-glutamine, 1% PenStrep, & 10% FBS). Cells were washed several times by centrifugation at 300*g for 5 min at 4 °C followed by resuspension in PBS with 1% BSA (PBS/1% BSA). Cells were resuspended between 5x10⁵ cells/ml to 2x10⁶ cell/ml and then distributed into a 96 well U-bottom plate. Diluted commercial antibody (0.25-2 μ g/ml), or hybridoma supernatants, or blood serum for polyclonal responses, were added to cells and incubated for 1 hr on ice. Following several washes with PBS/1% BSA, cells were incubated for 30 min on ice with a 1:1600 dilution of AlexaFluor647 conjugated F(ab)₂ goat anti-mouse IgG Fc γ (JacksonImmunoResearch). Cells were washed again with PBS/1% BSA and then fixed in 1% formaldehyde in PBS/1% BSA. Cells were analysed on either a 2 or 4 laser Attune NXT flow cytometer. Data was processed in FlowJo Software.

6.2.2.4 Immunofluorescence

[0419] Cells were seeded to 50% confluency in glass chamber slides (Nunc) and incubated 12-18 hours at 37 °C, 5% CO₂. Following overnight growth, media from slides was removed and

cells were fixed with 4% formaldehyde in PBS (pH 7.4) for 10 min at room temperature. Slides were washed in PBS. Diluted commercial antibody (1-4 µg/ml), or hybridoma supernatants, or blood serum for polyclonal responses, were added to the slides and the slides were incubated overnight at 4 °C. The slides were washed in PBS and stained with a 1:800 dilution of AlexaFluor488 conjugated F(ab)₂ rabbit anti-mouse IgG (H+L) (Invitrogen) for 45 min at room temperature. The slides were washed in PBS and mounted using Prolong Gold Antifade Mountant with DAPI (Thermofisher) and examined using an Olympus FV3000 confocal microscope.

6.2.3. Results

6.2.3.1 Glycopeptide specific antibodies to Tn-LAMP1

[0420] Glycopeptide reactive antibodies were generated using the Tn-glycosylated LAMP1 glycopeptide. Antibodies generated using LAMP1 glycopeptide, including 3C7, 13C3, and 13G2, proved superior in selectivity.

6.2.3.2 Binding specificities of mAb 3C7, 13C3, and 13G2

[0421] To characterize the binding specificities of 3C7, 13C3, and 13G2 for non-glycosylated and Tn-glycosylated LAMP1, flow cytometry analysis of the LAMP1 mouse antibodies on T47D COSMC-KO cells was performed. It was found that 3C7, 13C3, and 13G2 only reacted with Tn-glycosylated LAMP1 (e.g., T47D COSMC-KO cells) and not with its non-glycosylated counterpart (e.g., T47D cells) (FIGS. 1A and 1B-1 to 1B-5). The affinities of 3C7, 13C3, and 13G2 against the LAMP1 glycopeptides were determined by Biacore and Octet. Table 7 summarizes dissociation constants (K_d) for 3C7, 13C3, and 13G2 against different glycoforms of LAMP1 peptide, as well as unglycosylated LAMP1 and MUC1-Tn.

Table 7: Dissociation Constants (K_d) for 3C7.2C11.1C9, 13C3.1C8.1C9, and 13G2.1A10.2G5 against different glycoforms of LAMP1 peptide and unglycosylated LAMP1

	<i>Affinity (Biacore)</i>			<i>Apparent Affinity (Octet)</i>					
<i>Antibody</i>	<i>LAMP1-Tn</i>	<i>LAMP1</i>	<i>MUC1-Tn</i>	<i>LAMP1-Tn</i>	<i>LAMP1-Tn (S)</i>	<i>LAMP1-Tn (T1)</i>	<i>LAMP1-Tn (T2)</i>	<i>LAMP1</i>	<i>MUC1-Tn</i>
3C7	28.7 nM	>400 nM	>400 nM	18.2 nM	>10 μ M	0.81 μ M	>1 μ M	>10 μ M	>10 μ M
13C3	8.00 nM	>400 nM	>400 nM	3.46 nM	>10 μ M	0.23 μ M	>1 μ M	>10 μ M	>10 μ M
13G2	76.1 nM	>400 nM	>400 nM	17.5 nM	>10 μ M	0.57 μ M	>1 μ M	>10 μ M	>10 μ M

[0422] To further assess the specificities of 3C7, 13C3, and 13G2 in a more natural conformational context, 3C7, 13C3, and 13G2 was used to stain T47D cells for flow cytometry and immunofluorescence. T47D cell line is inherently Tn-negative but can be induced to express the Tn-antigen by KO of the COSMC chaperone. When using 3C7, 13C3, and 13G2 to stain for flow cytometry, it was found that each selectively stained COSMC KO T47D cells but not their wildtype counterpart, despite both cells staining positive for LAMP1 (FIG. 2). Immunofluorescence showed that only LAMP1⁺ Tn⁺ T47D COSMC KO cells stained with 3C7.2C11.1C9, 13C3.1C8.1C9, and 13G2.1A10.2G5, whereas LAMP1⁺ Tn⁻ T47D WT cells did not (FIG. 2).

6.3 Example 3: Comparison of specificity of 3C7, 13C3, and 13G2 antibodies relative to mAb237

6.3.1. Overview

[0423] It was discovered that antibodies 3C7, 13C3, and 13G2 are similar in sequence to the antibody mAb237 (see FIGS. 9A-9B). mAb237 is a recombinant mouse antibody (Creative Biolabs; Brooks *et al.*, 2010, Proc Natl Acad Sci USA. 107(22):10056-10061) having specificity for the Tn antigen ERG**I**KPPLEELSGK (SEQ ID NO:211; with O-linked GalNAc on the threonine residue shown with bold and underlined text), derived from podoplanin, no cross-reactivity to the non-glycosylated podoplanin peptide (Brooks *et al.*, 2010, Proc Natl Acad Sci USA. 107(22):10056-10061; Zhou *et al.*, 2018, Molecules. 23(6):1326). Because of the similarity in sequence between mAb237 and the LAMP1 anti-glyco-LAMP1 antibodies 3C7, 13C3, and 13G2, the inventors sought to determine whether there was any cross reactivity between mAb237 and the anti-glyco-LAMP1 antibodies of the disclosure.

6.3.2. Materials and Methods

6.3.2.1 Bio-Layer Interferometry (Octet)

[0424] Antibody affinity and epitope binning of monoclonal antibodies can be assessed against specific antigens using BLI. In a BLI assay, the antigen can be immobilized onto a biosensor (e.g., the LAMP1-Tn peptide Biotin-CEQDRP**SPTT**APPAPPSPSP (the amino acid portion of which is SEQ ID NO: 154; glycosylated with GalNAc on the serine and threonine residues shown in bold underlined text), a negative control analyte such as an unglycosylated LAMP1 peptide (Biotin-CEQDRPSPTTAPPAPPSPSP (the amino acid portion of which is SEQ ID NO: 155), or the podoplanin glycopeptide ERG**IK**PPLEELSGK (SEQ ID NO:211) (with O-linked GalNAc on the threonine residue shown with bold and underlined text)) and presented to one antibody for affinity measurements or two competing antibodies in tandem (or consecutive steps) for epitope binning. The binding to non-overlapping epitopes occurs if saturation with the first antibody does not block the binding of the second antibody. The affinity is determined by fitting the binding curve to a specific model: a 1:1 monovalent model or a 2:1 bivalent model. The error (>95% confidence) is calculated by how close the generated curve matches the model.

6.3.3. Results

6.3.3.1 No cross reactivity between mAb237 and the anti-glyco-LAMP1 antibodies 3C7, 13C3, and 13G2

[0425] To characterize the cross-reactivity between mAb237 the anti-glyco-LAMP1 antibodies 3C7, 13C3, and 13G2, the affinities of mAb237, 3C7, 13C3, and 13G2 against the glycosylated LAMP1 peptide, the unglycosylated LAMP1 peptide, and the podoplanin glycopeptide were determined by Octet. Table 8 summarizes the dissociation constants (K_d) for mAb237, 3C7, 13C3, and 13G2 against the glycosylated LAMP1 peptide, the unglycosylated LAMP1 peptide, and the podoplanin glycopeptide. No cross reactivity was observed despite the sequence similarities observed between mAb237 and 3C7, 13C3, and 13G2.

Table 8: Dissociation Constants (K_d) for mAb237, 3C7, 13C3, and 13G2 against the glycosylated LAMP1 peptide, the unglycosylated LAMP1 peptide, and the podoplanin glycopeptide			
	Apparent Affinity (Octet)		
Antibody	LAMP1-Tn	LAMP1	Podoplanin glycopeptide
3C7	13.9 nM	>10 μ M	>10 μ M
13C3	1.46 nM	>10 μ M	>10 μ M
13G2	15.2 nM	>10 μ M	>10 μ M
mAb237	>10 μ M	>10 μ M	1.53 nM

6.4 Example 4: Tissue expression of Tn-glycosylated LAMP1 epitope recognized by 3C7, 13C3, and 13G2

6.4.1. Overview

[0426] 3C7, 13C3, and 13G2 were characterized by immunohistochemistry on various normal and cancer tissues.

6.4.2. Materials and methods

[0427] Paraffin embedded tissue micro arrays (TMAs) or tissue sections were de-paraffinized with xylene and ethanol, following antigen retrieval with citrate buffer (pH 6.0) and heated in microwave for 18 min. TMAs obtained from USBIOMAX and were stained with Ultra Vison Quanto Detection System HRP DAB. Briefly, TMAs were washed in TBS, incubated with mAb supernatant for 2 hours. After wash in TBS x 2, the TMAs was incubated with Primary Antibody Amplifier Quanto for 10 min. After wash in TBS, TMAs were incubated with HRP polymer quanto (10 min) followed by DAB chromogen. Slides were counterstained with hematoxylin, were dehydrated, and mounted.

6.4.3. Results

[0428] When staining formalin-fixed paraffin embedded tissue sections for immunohistochemistry, positive staining was observed with 3C7, 13C3, and 13G2 with strong staining in 2/10 prostate (FIG. 3 and Table 9) and for 13C3 strong cellular surface staining was observed on 11/110 breast (FIG. 4B-1 and 4B-2), 9/120 lung (FIG. 4B-1 and 4B-2). This staining pattern correlated with staining for normal LAMP1 expression, showing that LAMP1 expression in these carcinomas predicted reactivity to 3C7, 13C3, and 13G2. Importantly, no reactivity when using 3C7, 13C3, and 13G2 to stain healthy adjacent tissues was observed (FIG. 3 and FIGS 4A-1 to 4B-2). In conclusion, 3C7, 13C3, and 13G2 positively were found to react with several cancer tissue sections, but not their healthy counterparts.

Table 9: Statistics of positive and negative stained prostate cancer (TMA T195e) tissue

Antibody	Cases	Positive	Negative
3C7.2C11.1C9	9	6 (67%)	3 (33%)
13C3.1C8.1C9	9	6 (67%)	3 (33%)
13G2.1A10.2G5	9	6 (67%)	3 (33%)
Anti-LAMP1	9	6 (67%)	3 (33%)

[0429] The identity of each tissue in the TMA is set forth in Tables 10-14.

TABLE 10

Position	No.	Age	Sex	Organ/Anatomic Site	Pathology diagnosis	TNM	Grade
A1	1	65	M	Prostate	Adenocarcinoma	T2N0M0	Malignant
A2	2	75	M	Prostate	Adenocarcinoma	T4N1M1	Malignant
A3	3	57	M	Prostate	Adenocarcinoma	T2N0M0	Malignant
A4	4	66	M	Prostate	Adenocarcinoma	T3AN0M0	Malignant
A5	5	65	M	Prostate	Adenocarcinoma	T2N0M0	Malignant
A6	6	75	M	Prostate	Adenocarcinoma	T4N1M1	Malignant
A7	7	57	M	Prostate	Adenocarcinoma	T2N0M0	Malignant
A8	8	66	M	Prostate	Adenocarcinoma	T3AN0M0	Malignant
B1	9	80	M	Prostate	Adenocarcinoma	T3AN0M0	Malignant
B2	10	70	M	Prostate	Adenocarcinoma	T3N0M0	Malignant
B3	11	73	M	Prostate	Adenocarcinoma	T2BN0M0	Malignant
B4	12	76	M	Prostate	Adenocarcinoma	T2BN0M0	Malignant
B5	13	80	M	Prostate	Adenocarcinoma	T2BN0M0	Malignant
B6	14	70	M	Prostate	Adenocarcinoma	T3N0M0	Malignant
B7	15	73	M	Prostate	Adenocarcinoma	T2BN0M0	Malignant
B8	16	76	M	Prostate	Adenocarcinoma (sparse)	T2BN0M0	Malignant
C1	17	66	M	Prostate	Adenocarcinoma	T2N0M0	Malignant
C2	18	72	M	Prostate	Leiomyosarcoma	T2N0M0	Malignant
C3	19	35	M	Prostate	Prostate tissue	-	Normal
C4	20	22	M	Prostate	Prostate tissue	-	Normal
C5	21	66	M	Prostate	Adenocarcinoma	T2N0M0	Malignant
C6	22	72	M	Prostate	Leiomyosarcoma	T2N0M0	Malignant
C7	23	35	M	Prostate	Prostate tissue	-	Normal
C8	24	22	M	Prostate	Prostate tissue	-	Normal

TABLE 11

Position	No.	Age	Sex	Organ/Anatomic Site	Pathology diagnosis	TNM
A1	1	2	F	Liver	Normal liver tissue	normal
A2	2	50	F	Liver	Normal liver tissue	normal
A3	3	14	F	Liver	Normal liver tissue	normal
A4	4	35	F	Liver	Normal liver tissue	normal
A5	5	24	M	Liver	Normal liver tissue	normal
A6	6	21	F	Liver	Normal liver tissue	normal
A7	7	Fetus	F	Liver	Normal fetal liver tissue	normal
A8	8	35	M	Liver	Normal liver tissue	normal
B1	9	35	M	Liver	Normal liver tissue	normal
B2	10	40	M	Liver	Normal liver tissue	normal
B3	11	40	M	Liver	Normal liver tissue	normal
B4	12	38	M	Liver	Normal liver tissue	normal
B5	13	34	M	Liver	Normal liver tissue	normal
B6	14	27	M	Liver	Normal liver tissue	normal
B7	15	25	F	Liver	Normal liver tissue	normal
B8	16	42	F	Pancreas	Normal pancreas tissue	normal
C1	17	35	F	Pancreas	Normal pancreas tissue	normal
C2	18	1 mon.	M	Pancreas	Normal pancreas tissue	normal
C3	19	35	M	Pancreas	Normal pancreas tissue	normal
C4	20	38	F	Pancreas	Normal pancreas tissue	normal

TABLE 11						
Position	No.	Age	Sex	Organ/Anatomic Site	Pathology diagnosis	TNM
C5	21	56	M	Stomach	Normal stomach tissue	normal
C6	22	35	F	Stomach	Normal stomach tissue	normal
C7	23	35	M	Stomach	Normal stomach tissue	normal
C8	24	22	M	Stomach	Normal gastric mucosa tissue	normal
D1	25	40	M	Stomach	Normal stomach tissue	normal
D2	26	38	F	Stomach	Normal stomach tissue	normal
D3	27	35	M	Stomach	Normal stomach tissue	normal
D4	28	48	M	Stomach	Normal stomach tissue	normal
D5	29	52	F	Stomach	Normal stomach tissue	normal
D6	30	24	M	Esophagus	Normal esophagus tissue	normal
D7	31	21	F	Esophagus	Normal esophagus tissue (fibrous and connective tissue)	normal
D8	32	26	M	Esophagus	Normal esophagus tissue	normal
E1	33	22	M	Esophagus	Normal esophagus tissue	normal
E2	34	48	M	Esophagus	Normal esophagus tissue	normal
E3	35	59	M	Esophagus	Normal esophagus tissue	normal
E4	36	50	F	Colon	Normal colon tissue	normal
E5	37	49	M	Colon	Normal colon tissue	normal
E6	38	21	F	Colon	Normal colon tissue (fibrous and smooth muscle tissue)	normal
E7	39	35	M	Colon	Normal colon tissue	normal
E8	40	49	M	Intestine	Normal small intestine tissue (sparse)	normal
F1	41	35	F	Intestine	Normal small intestine tissue	normal
F2	42	40	M	Intestine	Normal small intestine tissue	normal
F3	43	38	F	Intestine	Normal small intestine tissue	normal
F4	44	42	F	Intestine	Normal small intestine tissue with necrosis	normal
F5	45	57	F	Intestine	Normal small intestine tissue	normal
F6	46	37	M	Intestine	Normal small intestine tissue	normal
F7	47	61	F	Intestine	Normal small intestine tissue	normal
F8	48	27	M	Intestine	Normal small intestine tissue	normal

TABLE 12 (FDA999x; Normal tissue array)						
Position	No.	Age	Sex	Organ/Anatomic Site	Pathology diagnosis	TNM
A1	1	42	M	Cerebrum	Cerebrum tissue	Normal
A2	2	53	M	Cerebrum	Cerebrum tissue	Normal
A3	3	37	M	Cerebrum	Cerebrum tissue	Normal

A4	4	26	M	Cerebellum	Cerebellum tissue	Normal
A5	5	45	M	Cerebellum	Cerebellum tissue	Normal
A6	6	35	M	Cerebellum	Cerebellum tissue	Normal
A7	7	43	M	Adrenal gland	Adrenal gland tissue	Normal
A8	8	18	F	Adrenal gland	Adrenal gland tissue	Normal
A9	9	23	M	Adrenal gland	Adrenal gland tissue	Normal
A10	10	25	F	Ovary	Ovary tissue	Normal
A11	11	19	F	Ovary	Ovary tissue	Normal
A12	12	40	F	Ovary	Ovary tissue	Normal
B1	13	23	M	Pancreas	Pancreas tissue (autolyzed)	Normal
B2	14	21	F	Pancreas	Pancreas tissue	Normal
B3	15	29	M	Pancreas	Pancreas tissue	Normal
B4	16	30	M	Lymph node	Lymph node tissue	Normal
B5	17	27	M	Lymph node	Lymph node tissue	Normal
B6	18	30	M	Lymph node	Lymph node tissue	Normal
B7	19	32	F	Hypophysis	Hypophysis tissue	Normal
B8	20	40	F	Hypophysis	Hypophysis tissue	Normal
B9	21	28	F	Hypophysis	Hypophysis tissue	Normal
B10	22	28	M	Testis	Testis tissue	Normal
B11	23	35	M	Testis	Testis tissue	Normal
B12	24	34	M	Testis	Testis tissue	Normal
C1	25	40	F	Thyroid gland	Thyroid gland tissue	Normal
C2	26	27	M	Thyroid gland	Thyroid gland tissue	Normal
C3	27	45	M	Thyroid gland	Thyroid gland tissue	Normal
C4	28	50	F	Breast	Breast tissue	Normal
C5	29	58	F	Breast	Breast tissue	Normal
C6	30	42	F	Breast	Breast tissue	Normal
C7	31	23	M	Spleen	Spleen tissue	Normal
C8	32	45	M	Spleen	Spleen tissue	Normal
C9	33	21	F	Spleen	Spleen tissue	Normal
C10	34	10	M	Tonsil	Tonsil tissue (Mucus gland)	Normal
C11	35	7	F	Tonsil	Tonsil tissue	Normal
C12	36	34	M	Tonsil	Tonsil tissue (fibrous tissue)	Normal
D1	37	21	F	Thymus gland	Thymus gland tissue	Normal
D2	38	15	F	Thymus gland	Thymus gland tissue	Normal
D3	39	23	M	Thymus gland	Thymus gland tissue	Normal
D4	40	21	F	Bone marrow	Bone marrow tissue	Normal
D5	41	22	M	Bone marrow	Bone marrow tissue	Normal
D6	42	21	F	Bone marrow	Bone marrow tissue	Normal
D7	43	47	M	Lung	Lung tissue	Normal
D8	44	19	M	Lung	Lung tissue	Normal
D9	45	21	F	Lung	Lung tissue	Normal
D10	46	35	M	Heart	Cardiac muscle tissue	Normal
D11	47	40	M	Heart	Cardiac muscle tissue	Normal
D12	48	21	F	Heart	Cardiac muscle tissue	Normal
E1	49	19	M	Esophagus	Esophagus tissue	Normal
E2	50	47	M	Esophagus	Esophagus tissue(smooth muscle)	Normal

E3	51	35	M	Esophagus	Esophagus tissue	Normal
E4	52	45	M	Stomach	Stomach tissue	Normal
E5	53	24	M	Stomach	Stomach tissue	Normal
E6	54	37	M	Stomach	Stomach tissue	Normal
E7	55	45	M	Small intestine	Small intestine tissue	Normal
E8	56	30	M	Small intestine	Small intestine tissue	Normal
E9	57	32	M	Small intestine	Small intestine tissue	Normal
E10	58	32	M	Colon	Colon tissue	Normal
E11	59	21	F	Colon	Colon tissue	Normal
E12	60	35	M	Colon	Colon tissue	Normal
F1	61	38	M	Liver	Liver tissue	Normal
F2	62	45	M	Liver	Liver tissue	Normal
F3	63	23	M	Liver	Liver tissue	Normal
F4	64	30	M	Salivary gland	Salivary gland tissue	Normal
F5	65	21	F	Salivary gland	Salivary gland tissue	Normal
F6	66	21	F	Salivary gland	Salivary gland tissue	Normal
F7	67	27	M	Kidney	Kidney tissue	Normal
F8	68	2	F	Kidney	Kidney tissue	Normal
F9	69	47	M	Kidney	Kidney tissue	Normal
F10	70	30	M	Prostate	Prostate tissue	Normal
F11	71	38	M	Prostate	Prostate tissue	Normal
F12	72	36	M	Prostate	Prostate tissue	Normal
G1	73	54	F	Uterus	Endometrium tissue	Normal
G2	74	40	F	Uterus	Endometrium tissue	Normal
G3	75	42	F	Uterus	Endometrium tissue	Normal
G4	76	46	F	Cervix	Cervix canals tissue	Normal
G5	77	54	F	Cervix	Cervix canals tissue	Normal
G6	78	37	F	Cervix	Cervix canals tissue	Normal
G7	79	32	M	Bladder	Bladder tissue	Normal
G8	80	35	M	Bladder	Bladder tissue	Normal
G9	81	34	M	Bladder	Bladder tissue	Normal
G10	82	21	M	Skeletal muscle	Skeletal muscle tissue	Normal
G11	83	25	M	Skeletal muscle	Skeletal muscle tissue	Normal
G12	84	40	M	Skeletal muscle	Skeletal muscle tissue	Normal
H1	85	21	M	Skin	Skin tissue(sparse)	Normal
H2	86	27	F	Skin	Skin tissue	Normal
H3	87	25	M	Skin	Skin tissue	Normal
H4	88	30	M	Nerve	Peripheral nerve tissue	Normal
H5	89	33	M	Nerve	Peripheral nerve tissue	Normal
H6	90	35	M	Nerve	Peripheral nerve tissue	Normal
H7	91	30	M	Artery	mesothelial tissue	Normal
H8	92	23	M	Pericardium	mesothelial tissue	Normal
H9	93	45	M	Pericardium	mesothelial tissue	Normal
H10	94	62	F	Eye	Cancer adjacent wall of eyeball (choroid)	AT

H11	95	42	M	Eye	Cancer adjacent wall of eyeball (choroid)	AT
H12	96	54	F	Eye	Cancer adjacent wall of eyeball	AT
I1	97	10	M	Larynx	Larynx tissue	Normal
I2	98	28	F	Larynx	Larynx tissue	Normal
I3	99	18	F	Larynx	Larynx tissue	Normal

TABLE 13 (LC121b; lung cancer array)						
Position	No.	Age	Sex	Organ/Anatomic Site	Pathology diagnosis	TNM
A1	1	63	F	Lung	Squamous cell carcinoma	T3N1M0
A2	2	68	M	Lung	Squamous cell carcinoma	T2N2M0
A3	3	66	M	Lung	Squamous cell carcinoma	T2N2M0
A4	4	66	M	Lung	Squamous cell carcinoma	T3N1M0
A5	5	63	F	Lung	Squamous cell carcinoma	T2N2M0
A6	6	65	M	Lung	Squamous cell carcinoma	T2N2M0
A7	7	60	M	Lung	Squamous cell carcinoma	T4N0M0
A8	8	68	M	Lung	Squamous cell carcinoma	T2N2M0
A9	9	71	M	Lung	Squamous cell carcinoma	T2N2M0
A10	10	66	M	Lung	Squamous cell carcinoma	T2N2M0
A11	11	56	M	Lung	Squamous cell carcinoma	T3N2M0
A12	12	70	M	Lung	Squamous cell carcinoma	T4N2M0
B1	13	77	M	Lung	Squamous cell carcinoma	T4N1M0
B2	14	56	F	Lung	Squamous cell carcinoma	T4N0M0
B3	15	53	M	Lung	Squamous cell carcinoma	T4N0M0
B4	16	64	M	Lung	Squamous cell carcinoma	T3N2M0
B5	17	46	M	Lung	Squamous cell carcinoma	T2N0M0
B6	18	64	M	Lung	Squamous cell carcinoma	T4N0M0
B7	19	42	M	Lung	Squamous cell carcinoma	T3N1M0
B8	20	60	F	Lung	Squamous cell carcinoma	T2N2M0
B9	21	54	F	Lung	Large cell carcinoma	T2N1M0
B10	22	69	F	Lung	Large cell carcinoma	T3N0M0
B11	23	46	F	Lung	Large cell carcinoma	T2N0M0
B12	24	58	M	Lung	Large cell carcinoma	T2N0M0
C1	25	44	M	Lung	Large cell carcinoma	T1N0M0
C2	26	61	M	Lung	Large cell carcinoma	T4N0M0
C3	27	64	M	Lung	Large cell carcinoma	T2N0M0
C4	28	65	M	Lung	Large cell carcinoma	T2N0M0
C5	29	68	M	Lung	Large cell carcinoma (sparse)	T4N0M0
C6	30	31	M	Lung	Large cell carcinoma	T2N0M0
C7	31	58	M	Lung	Large cell carcinoma	T2N1M0
C8	32	58	M	Lung	Large cell carcinoma	T2N0M0
C9	33	60	M	Lung	Large cell carcinoma	T3N2M0
C10	34	40	M	Lung	Large cell carcinoma	T2N0M0
C11	35	60	M	Lung	Large cell carcinoma	T2N1M0
C12	36	49	M	Lung	Large cell carcinoma	T3N0M0
D1	37	65	F	Lung	Large cell carcinoma (sparse)	T2N1M0
D2	38	60	M	Lung	Large cell carcinoma	T2N0M0
D3	39	45	F	Lung	Large cell carcinoma	T2N0M0
D4	40	45	M	Lung	Large cell carcinoma	T1N0M0

D5	41	69	F	Lung	Large cell carcinoma	T2N0M0
D6	42	64	F	Lung	Large cell carcinoma	T2N0M0
D7	43	57	F	Lung	Large cell carcinoma	T2N0M0
D8	44	62	M	Lung	Large cell carcinoma	T2N0M0
D9	45	54	M	Lung	Large cell carcinoma	T2N0M0
D10	46	39	M	Lung	Large cell carcinoma	T2N0M0
D11	47	40	M	Lung	Large cell carcinoma	T2N0M0
D12	48	70	M	Lung	Large cell carcinoma	T3N1M0
E1	49	56	M	Lung	Large cell carcinoma	T2N1M0
E2	50	54	M	Lung	Large cell carcinoma	T2N1M0
E3	51	51	M	Lung	Large cell carcinoma	T2N0M0
E4	52	65	M	Lung	Large cell carcinoma	T2N0M0
E5	53	30	F	Lung	Large cell carcinoma	T2N1M0
E6	54	47	F	Lung	Large cell carcinoma	T2N2M0
E7	55	73	M	Lung	Large cell carcinoma (sparse)	T3N1M0
E8	56	51	M	Lung	Large cell carcinoma	T4N0M0
E9	57	60	M	Lung	Adenocarcinoma	T2N2M0
E10	58	49	M	Lung	Adenocarcinoma	T2N0M0
E11	59	52	M	Lung	Adenocarcinoma	T3N1M0
E12	60	46	F	Lung	Adenocarcinoma	T4N0M0
F1	61	62	F	Lung	Adenocarcinoma	T4N0M0
F2	62	56	M	Lung	Adenocarcinoma	T2N2M0
F3	63	54	F	Lung	Adenocarcinoma	T3N0M0
F4	64	61	M	Lung	Adenocarcinoma	T2N2M0
F5	65	62	M	Lung	Adenocarcinoma	T3N0M0
F6	66	36	F	Lung	Adenocarcinoma	T2N2M0
F7	67	41	M	Lung	Adenocarcinoma	T4N0M0
F8	68	66	M	Lung	Adenocarcinoma	T2N2M0
F9	69	64	M	Lung	Adenocarcinoma	T3N1M0
F10	70	68	F	Lung	Adenocarcinoma	T2N2M0
F11	71	60	M	Lung	Adenocarcinoma	T2N0M0
F12	72	42	M	Lung	Adenocarcinoma	T3N1M0
G1	73	35	M	Lung	Adenocarcinoma	T3N2M0
G2	74	62	M	Lung	Adenocarcinoma	T3N1M0
G3	75	65	F	Lung	Adenocarcinoma	T3N1M0
G4	76	54	F	Lung	Adenocarcinoma	T3N1M0
G5	77	46	M	Lung	Adenocarcinoma	T3N2M0
G6	78	72	M	Lung	Adenocarcinoma	T2N2M0
G7	79	56	M	Lung	Adenocarcinoma	T4N0M0
G8	80	30	F	Lung	Adenocarcinoma	T4N1M1
G9	81	48	M	Lung	Adenocarcinoma	T2N0M0
G10	82	47	F	Lung	Adenocarcinoma	T2N0M0
G11	83	69	M	Lung	Adenocarcinoma	T2N0M0
G12	84	65	M	Lung	Adenocarcinoma	T3N0M0
H1	85	60	F	Lung	Adenocarcinoma	T3N0M0
H2	86	22	F	Lung	Adenocarcinoma	T3N0M0
H3	87	55	F	Lung	Adenocarcinoma	T2N0M0
H4	88	43	F	Lung	Adenocarcinoma	T2N0M0
H5	89	50	F	Lung	Adenocarcinoma	T3N0M0
H6	90	49	F	Lung	Adenocarcinoma	T2N0M0
H7	91	47	F	Lung	Adenocarcinoma	T2N0M0
H8	92	50	M	Lung	Adenocarcinoma	T2N1M0
H9	93	82	M	Lung	Adenocarcinoma	T4N1M0

H10	94	54	F	Lung	Adenocarcinoma	T4N1M0
H11	95	38	M	Lung	Adenocarcinoma	T4N1M0
H12	96	57	M	Lung	Adenocarcinoma	T4N0M0
I1	97	42	M	Lung	Adenocarcinoma	T3N1M0
I2	98	65	M	Lung	Adenocarcinoma	T3N2M0
I3	99	59	M	Lung	Adenocarcinoma	T4N3M0
I4	100	62	M	Lung	Adenocarcinoma	T4N0M0
I5	101	49	F	Lung	Adenocarcinoma	T2N0M0
I6	102	39	M	Lung	Adenocarcinoma	T4N0M0
I7	103	42	F	Lung	Adenocarcinoma	T3N1M0
I8	104	60	F	Lung	Adenocarcinoma	T4N0M0
I9	105	42	F	Lung	Adenocarcinoma	T4N1M0
I10	106	54	F	Lung	Adenocarcinoma	T2N0M0
I11	107	50	M	Lung	Papillary adenocarcinoma	T3N1M0
I12	108	51	M	Lung	Papillary adenocarcinoma	T2N0M0
J1	109	47	F	Lung	Papillary adenocarcinoma	T3N1M0
J2	110	53	F	Lung	Papillary adenocarcinoma	T2N0M0
J3	111	56	M	Lung	Adjacent normal lung tissue	-
J4	112	57	M	Lung	Adjacent normal lung tissue	-
J5	113	51	F	Lung	Adjacent normal lung tissue	-
J6	114	68	M	Lung	Adjacent normal lung tissue	-
J7	115	53	F	Lung	Adjacent normal lung tissue	-
J8	116	45	M	Lung	Adjacent normal lung tissue	-
J9	117	27	M	Lung	Lung tissue	-
J10	118	15	F	Lung	Lung tissue	-
J11	119	48	M	Lung	Lung tissue	-
J12	120	16	F	Lung	Lung tissue	-

TABLE 14 (BC08013d; breast cancer array)

Position	No.	Age	Sex	Organ/Anatomic Site	Pathology diagnosis	TNM
A1	1	35	F	Breast	Invasive ductal carcinoma	T1N0M0
A2	2	54	F	Breast	Invasive ductal carcinoma	T3N0M0
A3	3	74	F	Breast	Invasive ductal carcinoma	T4N0M0
A4	4	38	F	Breast	Invasive ductal carcinoma	T2N1M0
A5	5	47	F	Breast	Invasive ductal carcinoma	T2N0M0
A6	6	44	F	Breast	Invasive ductal carcinoma	T4N0M0

A7	7	37	F	Breast	Invasive ductal carcinoma	T2N0M0
A8	8	42	F	Breast	Invasive ductal carcinoma	T4N0M0
A9	9	41	F	Breast	Invasive ductal carcinoma	T2N0M0
B1	10	55	F	Breast	Invasive ductal carcinoma	T4N1M0
B2	11	79	F	Breast	Invasive ductal carcinoma	T4N0M0
B3	12	45	F	Breast	Invasive ductal carcinoma	T4N2M0
B4	13	48	F	Breast	Invasive ductal carcinoma	T4N2M0
B5	14	50	F	Breast	Invasive ductal carcinoma	T2N0M0
B6	15	44	F	Breast	Invasive ductal carcinoma	T2N0M0
B7	16	38	F	Breast	Invasive ductal carcinoma	T2N0M0
B8	17	50	F	Breast	Invasive ductal carcinoma	T2N1M0
B9	18	49	F	Breast	Invasive ductal carcinoma	T4N1M0
C1	19	45	F	Breast	Invasive ductal carcinoma	T1N0M0
C2	20	47	F	Breast	Invasive ductal carcinoma	T4N0M0
C3	21	61	F	Breast	Invasive ductal carcinoma	T2N0M0
C4	22	48	F	Breast	Invasive ductal carcinoma	T4N0M0
C5	23	68	F	Breast	Invasive ductal carcinoma	T2N1M0
C6	24	53	F	Breast	Invasive ductal carcinoma	T2N0M0
C7	25	42	F	Breast	Invasive ductal carcinoma	T3N0M0
C8	26	52	F	Breast	Invasive ductal carcinoma	T3N0M0
C9	27	50	F	Breast	Invasive ductal carcinoma	T2N1M0
D1	28	38	F	Breast	Invasive ductal carcinoma	T2N0M0
D2	29	35	F	Breast	Invasive ductal carcinoma	T2N0M0
D3	30	32	F	Breast	Invasive ductal carcinoma	T1N1M0
D4	31	38	F	Breast	Invasive ductal carcinoma	T3N0M0
D5	32	52	F	Breast	Invasive ductal carcinoma	T3N0M0
D6	33	31	F	Breast	Invasive ductal carcinoma	T2N0M0
D7	34	41	F	Breast	Invasive ductal carcinoma	T2N0M0
D8	35	54	F	Breast	Invasive ductal carcinoma	T2N1M0
D9	36	63	F	Breast	Invasive ductal carcinoma	T2N0M0
E1	37	52	F	Breast	Invasive ductal carcinoma	T2N0M0
E2	38	58	F	Breast	Invasive ductal carcinoma	T2N0M0
E3	39	48	F	Breast	Invasive ductal carcinoma (breast tissue)	T1N0M0
E4	40	40	F	Breast	Invasive ductal carcinoma	T3N0M0
E5	41	40	F	Breast	Invasive ductal carcinoma	T2N2M0
E6	42	57	F	Breast	Invasive ductal carcinoma	T4N2M0
E7	43	28	F	Breast	Invasive ductal carcinoma	T1N1M0
E8	44	46	F	Breast	Invasive ductal carcinoma	T1N0M0
E9	45	38	F	Breast	Invasive ductal carcinoma	T4N0M0
F1	46	59	F	Breast	Invasive ductal carcinoma	T2N2M0
F2	47	47	F	Breast	Invasive ductal carcinoma	T3N0M0
F3	48	48	F	Breast	Invasive ductal carcinoma	T4N0M0
F4	49	50	F	Breast	Invasive ductal carcinoma	T4N0M0
F5	50	48	F	Breast	Invasive ductal carcinoma	T2N1M0
F6	51	46	F	Breast	Invasive ductal carcinoma	T2N0M0
F7	52	37	F	Breast	Invasive ductal carcinoma	T2N1M0
F8	53	76	F	Breast	Invasive ductal carcinoma	T4N0M0
F9	54	52	F	Breast	Invasive ductal carcinoma	T2N0M0
G1	55	55	F	Breast	Invasive ductal carcinoma	T2N0M0
G2	56	46	F	Breast	Invasive ductal carcinoma	T2N1M0
G3	57	45	F	Breast	Invasive ductal carcinoma	T2N0M0
G4	58	62	F	Breast	Invasive ductal carcinoma	T2N1M0
G5	59	41	F	Breast	Invasive ductal carcinoma	T2N0M0

G6	60	51	F	Breast	Invasive ductal carcinoma	T3N1M0
G7	61	59	F	Breast	Medullary carcinoma	T3N0M0
G8	62	56	F	Breast	Medullary carcinoma	T2N0M0
G9	63	52	F	Breast	Medullary carcinoma	T2N0M0
H1	64	40	F	Breast	Medullary carcinoma	T1N0M0
H2	65	46	F	Breast	Medullary carcinoma	T3N0M0
H3	66	41	F	Breast	Medullary carcinoma	T2N1M0
H4	67	35	F	Breast	Medullary carcinoma	T2N0M0
H5	68	55	F	Breast	Medullary carcinoma	T2N0M0
H6	69	39	F	Breast	Medullary carcinoma	T2N1M0
H7	70	49	F	Breast	Adjacent normal breast tissue (fibrofatty tissue and blood vessel)	-
H8	71	38	F	Breast	Adjacent normal breast tissue (fibrofatty tissue and blood vessel)	-
H9	72	43	F	Breast	Adjacent normal breast tissue (fibrofatty tissue and blood vessel)	-

6.5 Example 5: Tn-LAMP1 based CARs

6.5.1. Overview

[0430] Chimeric antigen receptors (CARs) having VH and VL domains of 3C7.2C11.1C9, 13C3.1C8.1C9, and 13G2.1A10.2G5 were designed. CARs were then evaluated in target-specific a cytotoxicity assay.

6.5.2. Materials and Methods

6.5.2.1 Vector Design

[0431] Various CAR constructs having scFvs having VH and VL domains of 3C7, 13C3, and 13G2 were designed (FIGS 8A-8C). In the constructs, the VH and VL are attached together with one long linker (GGGGS)₃ (SEQ ID NO:160) to the CD8a hinge followed by a second generation CAR-T (CD28 intracellular signal domain, and a CD3-zeta intracellular chain). The N-terminus of the scFvs was attached to a CD8a signal sequence. The LAMP1 CAR-Ts were subcloned into the Virapower lentivirus vector pLENTI6.3-V5-DEST (Invitrogen). Nucleotide sequences encoding the CARs are shown in Table 15. Amino acid sequences of the CARs are shown in Table 16.

Table 15: Nucleotide sequences encoding LAMP1 base CARs			
Construct	Nucleotide Sequence	Nucleic Acid description	SEQ ID No.
3C7-CART	ATGGCTCTGCCCGTTACAGCTCTGCTGCTG CCTCTGGCTCTGCTTCTGCATGCCGCTAGA CCCGACGTGATGCTGACACAGACACCTCTG AGCCTGCCTGTGTCTCTGGGAGATCAGGCC AGCATCAGCTGCAGATCTAGCCAGAGCCTG GTGCACAGCAACGGCAACACATACCTGCAC TGGTATCTGCAGAAGCCCGGACAGAGCCCC AAGCTGCTGATCAACAAGGTGTCCAACCGG	1-63 = CD8A signal sequence 64-399 = 3C7 LC 400-444 = Linker 445-801 = 3C7 HC	202

Table 15: Nucleotide sequences encoding LAMP1 base CARs		
	TTCTTCGGCGTGCCCGATAGATTTTCTGGCA GCGGCTCTGGCACCAGCTTCACCCTGAAGA TCAGCAGAGTGGAAGCCGAGGACCTGGGC GTGTACTTCTGTAGCCAGTCTACCCACGTG CCACGGACATTTGGCGGCGGAACAAAGCTG GAAATCAAAGGCGGCGGAGGATCTGGCGG AGGTGGAAGTGGCGGAGGCGGATCTGAAG TGAAGCTGGAAGAATCAGGCGGAGGCCTG GTTCAGCCTGGCGGCTCTATGAAGGTTTCC TGTGGCGCCAGCGGCTTCACCTTTTCCGAT GCCTGGATGGACTGGGTCCGACAGTCTCCT GAGAAAGGCCTGGAATGGGTGCGCCGAGAT GAGAAGCAAGGCCTTCAACCACGCCATCTA CTACGCCGAGAGCGTGAAGGGCAGATTCAC CATCAGCCGGGACGACAGCAAGAGCAGAG TGTACCTGCAGATGAACCTGCTGAGGCCCCG AGGACACCGGCATCTACTATTGCACCCCTA ACTGGGACGAGGGCTTCGCCTATTGGGGAC AGGGAACACTGGTCACCGTGTCCGCCACAA CAACCCCTGCTCCTAGACCTCCTACACCAG CTCCTACAATCGCCTCTCAACCTCTGTCTCT GCGGCCTGAGGCTTGTAGACCTGCTGCTGG CGGAGCCGTGCATACAAGAGGACTGGATTT CGCCTGCGACTTCTGGGTGCTCGTGTTGT TGGCGGAGTGCTGGCTTGTACTCCCTGCT GGTCACAGTGCCCTTCATCATCTTTTGGGTG CGAAGCAAGCGGAGCCGGCTGCTGCACAG CGACTACATGAACATGACCCCTAGACGGCC CGGACCTACCAGAAAGCACTACCAGCCTTA CGCTCCTCCTAGAGACTTCGCCGCCTACCG GTCCAGAGTGAAGTTCTCCAGATCCGCTGA TGCCCTGCCTATCAGCAGGGACAGAACCA GCTGTACAACGAGCTGAACCTGGGGAGAAG AGAAGAGTACGACGTGCTGGACAAGCGGA GAGGCAGAGATCCTGAGATGGGCGGCAAG CCCAGACGGAAGAATCCTCAAGAGGGCCTG TATAATGAGCTGCAGAAAGACAAGATGGCC GAGGCCTACAGCGAGATCGGAATGAAGGG CGAGCGCAGAAGAGGCAAGGGACACGATG GACTGTACCAGGGCCTGAGCACCGCCACCA AGGATACCTATGATGCCCTGCACATGCAGG CCCTGCCTCCAAGAAGAAAAAGAGGCAGCG GCGAAGGCAGAGGCTCTCTGCTTACATGTG GCGACGTGGAAGAGAACCCCGGACCAATG GTGTCCAAGGGCGAAGAGGACAACATGGC CATCATCAAAGAATTCATGCGGTTCAAGGTG CACATGGAAGGCAGCGTGAACGGCCACGA GTTCGAGATTGAAGGCGAAGGCGAGGGCA GACCTTACGAGGGAACACAGACCGCCAAGC TGAAAGTGACCAAAGGCGGACCCCTGCCTT TCGCCTGGGATATCCTGTCTCCTCAGTTTAT GTACGGCTCCAAGGCCTACGTGAAGCACCC CGCCGATATTCCCGACTACCTGAAGCTGAG CTTCCCTGAGGGCTTCAAGTGGGAGAGAGT GATGAACCTTCGAGGACGGCGGCGTCTGTA CCGTGAAGTCAAGATAGCTCTCTGCAGGACG GCGAGTTTCTCTACAAAGTGAACTGCGGG GCACCAACTTTCCAGCGACGGCCCTGTGA TGCAGAAAAAGACCATGGGCTGGGAAGCCA GCAGCGAGAGAATGTACCCAGAAGATGGCG CCCTGAAAGGCGAGATCAAGCAGCGGCTGA AACTGAAGGATGGCGGCCACTACGACGCC	802-936 = CD8a hinge 937- 1017 = CD28 transmembrane domain 1018- 1140 = intracellular signal domain 1141- 1476 = CD3-zeta intracellular chain 1477- 2259= T2A-mCherry

Table 15: Nucleotide sequences encoding LAMP1 base CARs			
	GAAGTGAAAACACCTACAAGGCCAAGAAA CCCGTGCAGCTGCCTGGCGCCTACAACGTG AACATCAAGCTGGACATCACCAGCCACAAC GAGGACTACACCATCGTGGAACAGTACGAG AGAGCCGAAGGCAGGCACTCTACAGGCGG AATGGACGAGCTGTATAAGTAG		
13C3- CART	ATGGCTCTGCCGTTACAGCTCTGCTGCTG CCTCTGGCTCTGCTTCTGCATGCCGCCAGA CCTGACGTGGTCATGACACAGACACCTCTG AGCCTGCCTGTGTCTCTGGGAGATCAGGCC AGCATCAGCTGCAGATCTAGCCAGAGCCTG GTGCACAGCAACGGCAACACATACCTGCAC TGGTATCTGCAGAAGCCCGGACAGAGCCCC AAGCTGCTGATCAACAAGGTGTCCAACCGG TTCAGCGGCGTGCCCGATAGATTTTCTGGC AGCGGCTCTGGCACCGACTTCACCCTGAAG ATCAGCAGAGTGGAAGCCGAGGACCTGGG CGTGTACTTCTGTAGCCAGTCTACCCACGT GCCACGGACATTTGGCGGCGGAACAAAGCT GGAAATCAAAGGCGGCGGAGGATCTGGCG GAGGTGGAAGTGCGGAGGCGGATCTGAA GTGAAGCTGGAAGATTCAGGCGGAGGCCT GGTTCAGCCTGGCGGATCTATGAAGCTGAG CTGTGCCGCCAGCGGCTTCACCTTTTCTGA CGCCTGGATGGACTGGGTCCGACACTCTCC TGAGAAAGGCCGTGGAATGGGTGCGCCGAGCT GAGAAGCAAGGCCTTCAATCACGCCACCTA CTACGCCGAGAGCGTGAAGGGCAGATTAC CATCAGCCGGGACGACAGCAAGAGCACCG TGTAACCTGCAGATGAACAGCCTGAGAGCCG AGGATACCGGCATCTACTACTGCACCCCTA ACTGGGATGAGGGCTTCGCCTATTGGGGCC AGGGAACACTGGTTACCGTGTCCGCCACAA CAACCCCTGCTCCTAGACCTCCTACACCAG CTCCTACAATCGCCTCTCAACCTCTGTCTCT GCGGCCTGAGGCTTGTAGACCTGCTGCTGG CGGAGCCGTGCATACAAGAGGACTGGATTT CGCCTGCGACTTCTGGGTGCTCGTGGTTGT TGGCGGAGTGCTGGCTTGTTACTCCCTGCT GGTCACCGTGCCCTTCATCATCTTTTGGGT CCGAAGCAAGCGGAGCCGGCTGCTGCACA GCGACTACATGAACATGACCCCTAGACGGC CCGGACCTACCAGAAAGCACTACCAGCCTT ACGCTCCTCCTAGAGACTTCGCCGCCTACC GGTCCAGAGTGAAGTTCTCCAGATCCGCTG ATGCCCCTGCCTATCAGCAGGGACAGAACC AGCTGTACAACGAGCTGAACCTGGGGAGAA GAGAAGAGTACGACGTGCTGGACAAGCGG AGAGGCAGAGATCCTGAGATGGGCGGCAA GCCCAGACGGAAGAATCCTCAAGAGGGCCT GTATAATGAGCTGCAGAAAGACAAGATGGC CGAGGCCTACAGCGAGATCGGAATGAAGG GCGAGCGCAGAAGAGGCAAGGGACACGAT GGACTGTACCAGGGCCTGAGCACCGCCAC CAAGGATACCTATGATGCCCTGCACATGCA GGCCCTGCCTCCAAGAAGAAAAAGAGGCAG CGGCGAAGGCAGAGGCTCTCTGCTTACATG TGGCGACGTGGAAGAGAACCCCGGACCAAT GGTGTCCAAGGGCGAAGAGGACAACATGG CCATCATCAAAGAATTCATGCGGTTCAAGGT GCACATGGAAGGCAGCGTGAACGGGCCACG AGTTCGAGATAGAAGGCGAAGGCGAGGGC	1-63 = CD8A signal sequence 64-399 = 13C3 LC 400-444 = Linker 445-801 = 13C3 HC 802-936 = CD8a hinge 937- 1017 = CD28 transmembrane domain 1018- 1140 = intracellular signal domain 1141- 1476 = CD3-zeta intracellular chain 1477- 2259= T2A-mCherry	203

Table 15: Nucleotide sequences encoding LAMP1 base CARs			
	AGACCTTACGAGGGAACACAGACCGCCAAG CTGAAAGTGACCAAAGGCGGACCCCTGCCT TTCGCCTGGGATATCCTGTCTCCTCAGTTTA TGTACGGCTCCAAGGCCTACGTGAAGCACC CCGCCGATATTCCTGACTACCTGAACTGA GCTTCCCCGAGGGCTTCAAGTGGGAGAGA GTGATGAACTTCGAGGACGGCGGCGTCGT GACCGTGAAGTCAAGATAGCTCTCTGCAGGA CGGCGAGTTCATCTACAAAGTGAACTGCG GGGCACCAACTTTCCAGCGACGGCCCTGT GATGCAGAAAAAGACCATGGGCTGGGAAGC CAGCAGCGAGAGAATGTACCCAGAAGATGG CGCCCTGAAAGGCGAGATCAAGCAGCGGC TGAAGCTGAAGGATGGCGGCCACTACGACG CCGAAGTGAAAACCACTACAAGGCCAAGA AACCCGTGCAGCTGCCTGGCGCCTACAACG TGAACATCAAGCTGGACATCACCAGCCACA ACGAGGACTACACCATCGTGGAACAGTACG AGAGAGCCGAAGGCAGGCACTCTACAGGC GGAATGGACGAGCTGTATAAGTAG		
13G2-CART	ATGGCTCTGCCCCTTACAGCTCTGCTGCTG CCTCTGGCTCTGCTTCTGCATGCCGCCAGA CCTGACGTGGTCATGACACAGATCCCTCTG AGCCTGTGTGTGTCCCTGGGAGATCAGGCC AGCATCAGCTGTAGAAGCAGCCAGAGCCTG GTGCACAACAACGGCAACACCTACCTGCAC TGGTATCTGCAGAAGCCCGACAGAGCCCC AAGCTGCTGATCAACAAGGTGTCCAAGCGG TTCACCGGCGTGCCCGATAGATTTTCTGGC AGCGGCTCTGGCACCGACTTCACCCTGAAG ATCAGCAGAGTGGAAGCCGAGGACCTGGG CGTGTACTTCTGTAGCCAGAGCACCCACGT GCCAAGAACCCTTTGGCGGCGGAACAAAGCT GGAAATCAAAGGCGGCGGAGGATCTGGCG GAGGTGGAAGTGCGGAGGCGGATCTGAA GTTTCGGCTGGAAGAATCAGGTGGCGGACTG GTTCAACCTGGCGGCTCTATGAAGCTGAGC TGTGTGGCCAGCGGCTTCACCTTTTCCGAC GCCTGGATGGACTGGGTCCGACAGTCTCCT GAACGCGGCCCTTGAATGGGTGCGGAGCTG AGAAGCAAGACCTTCAACCACGCCACCTAC TACGCCGAGTCTGTGCGGGGCAGATTACCC ATCTCCAGAGATGACAGCAAGAGCACCGTG TACCTGCAGATGAACAGCCTGAGAGCCGAG GATACCGGCATCTACTACTGCAGCCCCAAC TGGGATGAGGGCTTTGCCTATTGGGGCCAG GGCACACTGGTTACCGTGTCTGCCACAACA ACCCCTGCTCCTAGACCTCCTACACCAGCT CCTACAATCGCCTCTCAACCTCTGTCTCTGC GGCCTGAGGCTTGTAGACCTGCTGCTGGCG GAGCCGTGCATACAAGAGGACTGGATTTTCG CCTGCGACTTCTGGGTGCTCGTGGTTGTTG GCGGAGTGCTGGCTTGTTACTCCCTGCTGG TCACCGTGGCCTTCATCATCTTTTGGGTCCG AAGCAAGCGGAGCCGGCTGCTGCACAGCG ACTACATGAACATGACCCCTAGACGGCCCG GACCTACCAGAAAGCACTACCAGCCTTACG CTCCTCCTAGAGACTTCGCCGCCTACCGGT CCAGAGTGAAGTTCTCCAGATCCGCTGATG CCCCTGCCTATCAGCAGGGACAGAACCAGC TGTACAACGAGCTGAACCTGGGGAGAAGAG AAGAGTACGACGTGCTGGACAAGCGGAGA	1-63 = CD8A signal sequence 64-399 = 13G2 LC 400-444 = Linker 445-801 = 13G2 HC 802-936 = CD8a hinge 937- 1017 = CD28 transmembrane domain 1018- 1140 = intracellular signal domain 1141- 1476 = CD3-zeta intracellular chain 1477- 2259= T2A-mCherry	204

Table 15: Nucleotide sequences encoding LAMP1 base CARs

GGCAGAGATCCTGAGATGGGCGGCAAGCC CAGACGGAAGAATCCTCAAGAGGGCCTGTA TAATGAGCTGCAGAAAGACAAGATGGCCGA GGCCTACAGCGAGATCGGAATGAAGGGCG AGCGCAGAAGAGGCAAGGGACACGATGGA CTGTACCAGGGCCTGAGCACCGCCACCAAG GATACCTATGATGCCCTGCACATGCAGGCC CTGCCTCCAAGAAGAAAAAGAGGCAGCGGC GAAGGCAGAGGCTCTCTGCTTACATGTGGC GACGTGGAAGAGAACCCCGGACCAATGGT GTCTAAGGGCGAAGAGGACAACATGGCCAT CATCAAAGAATTCATGCGGTTCAAGGTGCA CATGGAAGGCAGCGTGAACGGCCACGAGTT CGAGATTGAAGGCGAAGGCGAGGGCAGAC CTTACGAGGGAACACAGACCGCCAAGCTGA AAGTGACCAAAGGCGGACCCCTGCCTTTCG CCTGGGATATCCTGTCTCCTCAGTTTATGTA CGGCAGCAAGGCCTACGTGAAGCACCCCG CCGATATTCCCGACTACCTGAAACTGAGCTT CCCCGAGGGCTTCAAGTGGGAGAGAGTGAT GAACTTCGAGGACGGCGGCGTCGTGACCG TGACTCAAGATAGCTCTCTGCAGGACGGCG AGTTCATCTACAAAGTGAAGCTGCGGGGCA CCAACTTTCCCTCTGATGGCCCCGTGATGC AGAAAAAGACCATGGGCTGGGAAGCCAGCA GCGAGAGAATGTACCCAGAAGATGGCGCCC TGAAAGGCGAGATCAAGCAGCGGCTGAAGC TGAAGGATGGCGGCCACTACGACGCCGAA GTGAAAACCACTACAAGGCCAAGAAACCC GTGCAGCTGCCTGGCGCCTACAACGTGAAC ATCAAGCTGGACATCACCAGCCACAACGAG GACTACACCATCGTGGAACAGTACGAGAGA GCCGAAGGCAGGCACTCTACAGGCGGAAT GGACGAGCTGTATAAGTAG		
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Table 16: Amino Acid sequences encoding CAR-T

Construct	Amino Acid Sequence	Amino Acid Description	SEQ ID No.
3C7-CART	MALPVTALLLPLALLLHAARPDVMLTQTPL SLPVSLGDQASISCRSSQSLVHSNGNTYL HWYLQKPGQSPKLLINKVSNRFFGVPDR FSGSGSGTDFTLKISRVEAEDLGVFCSQ STHVPRTFGGGTKLEIKGGGSGGGGSG GGGSEVKLEESGGGLVQPGGSMKVSCG ASGFTFSDAWMDWWRQSPEKGLEWVAE MRSKAFNHAIYYAESVKGRFTISRDDSKS RVYLQMNLLRPEDTGIYYCTPNWDEGFA YWGQGLTVTSATTPAPRPPTPAPTIAS QPLSLRPEACRPAAGGAVHTRGLDFACD FWVLVWGGVLACYSLLVTVAFIIFWWRK RSRLHSDYMNMTPRRPGPTRKHYPYA PPRDFAAYSRVKFSRSADAPAYQQGQN QLYNELNLGRREEYDVLDKRRGRDPEMG GKPRRKNPQEGLYNELQKDKMAEAYSEI GMKGERRRGKGGHDGLYQGLSTATKDTY DALHMQALPPRRKRGSGEGRSLLTCGD VEENPGPMVSKGEEDNMAIKEFMRFKVH	1-21=CD8a signal sequence 22-133= 3C7 LC 134-148 = Linker 149-267 = 3C7 HC 268 -312 = CD8a hinge 313-3 CD28 transmembrane 340-380 CD28 intracellular domain 381-492 CD3z intracellular domain 381-752 = T2A mcherry	205

	Table 16: Amino Acid sequences encoding CAR-T		
	MEGSVNGHEFEIEGEGEGRPHYEGTQTAK LKVTKGGPLPFAWDILSPQFMYGSKAYVK HPADIPDYLKLSFPEGFKWERVMNFEDG GVVTVTQDSSLQDGEFIYKVKLRGTNFP DGPVMQKKTMGWEASSERMYPEDGALK GEIKQRLKLDGGHYDAEVKTTYKAKKP QLPGAYNVNIKLDITSHNEDYTIVEQYERA EGRHSTGGMDELYK*		
13C3-CART	MALPVTALLPLALLLHAARPDVMTQTPL SLPVSLGDQASISCRSSQSLVHSNGNTYL HWYLQKPGQSPKLLINKVSNRFSGVPDR FSGSGSGTDFTLKISRVEAEDLGVYFCSQ STHVPRTFGGGTKLEIKGGGGSGGGGSG GGGSEVKLEDSGGGLVQPGGSMKLSA ASGFTFSDAWMDWVRHSPEKGLEWVAE LRSAFNHATYYAESVKGRTISRDDSKS TVYLQMNSLRAEDTGIYYCTPNWDEGFA YWGQGTLLTVSATTTAPRPPTPAPTAS QPLSLRPEACRPAAGGAVHTRGLDFACD FWVLVWVGVLACYSLLVTVAFIIFWVRSK RSRLHSDYMNMTPRRPGPTRKHYPYA PPRDFAAYSRVKFSRSADAPAYQQGQN QLYNELNLGRREEYDVLDRGRDPEMG GKPRRKNPQEGLYNELQKDKMAEAYSEI GMKGERRRGKGGHDGLYQGLSTATKDTY DALHMQALPPRRKRGSGEGRGSLLTCGD VEENPGPMVSKGEEDNMAIIEFMRFKVH MEGSVNGHEFEIEGEGEGRPHYEGTQTAK LKVTKGGPLPFAWDILSPQFMYGSKAYVK HPADIPDYLKLSFPEGFKWERVMNFEDG GVVTVTQDSSLQDGEFIYKVKLRGTNFP DGPVMQKKTMGWEASSERMYPEDGALK GEIKQRLKLDGGHYDAEVKTTYKAKKP QLPGAYNVNIKLDITSHNEDYTIVEQYERA EGRHSTGGMDELYK*	1-21=CD8a signal sequence 22-133= 13C3 LC 134-148 = Linker 149-267 = 13C3 HC 269 -312 = CD8a hinge 313-339 CD28 transmembrane 340-380 CD28 intracellular domain 381-492 CD3z intracellular domain 381-752 = T2A mcherry	206
13G2-CART	MALPVTALLPLALLLHAARPDVMTQIPL SLCVSLGDQASISCRSSQSLVHNNGNTYL HWYLQKPGQSPKLLINKVSKRFTGVPDRF SGSGSGTDFTLKISRVEAEDLGVYFCSQS THVPRTFGGGTKLEIKGGGGSGGGGSG GGGSEVRLEESGGGLVQPGGSMKLSA ASGFTFSDAWMDWVRQSPERGLEWVAE LRSKTFNHATYYAESVRGRFTISRDDSKS TVYLQMNSLRAEDTGIYYCSPNWDEGFA YWGQGTLLTVSATTTAPRPPTPAPTAS QPLSLRPEACRPAAGGAVHTRGLDFACD FWVLVWVGVLACYSLLVTVAFIIFWVRSK RSRLHSDYMNMTPRRPGPTRKHYPYA PPRDFAAYSRVKFSRSADAPAYQQGQN QLYNELNLGRREEYDVLDRGRDPEMG GKPRRKNPQEGLYNELQKDKMAEAYSEI GMKGERRRGKGGHDGLYQGLSTATKDTY DALHMQALPPRRKRGSGEGRGSLLTCGD VEENPGPMVSKGEEDNMAIIEFMRFKVH MEGSVNGHEFEIEGEGEGRPHYEGTQTAK	1-21=CD8a signal sequence 22-133= 13G2 LC 134-148 = Linker 149-267 = 13G2 HC 268 -312 = CD8a hinge 313-339 CD28 transmembrane 340-380 CD28 intracellular domain 381-492 CD3z intracellular domain 381-752 = T2A mcherry	207

	Table 16: Amino Acid sequences encoding CAR-T		
	LKVTKGGPLPFAWDILSPQFMYGSKAYVK HPADIPDYLKLSFPEGFKWERVMNFEDG GVVTVTQDSSLQDGEFIYKVKLRGTNFP DGPVMQKKTMGWEASSERMYPEDGALK GEIKQRLKLDGGHYDAEVKTTYKAKKPV QLPGAYNVNIKLDITSHNEDYTIVEQYERA EGRHSTGGMDELYK		

6.5.3. Results

[0432] CAR constructs were expressed in human T cells. Surface expression of CART constructs was confirmed by flow cytometry using Alexa488-ProteinL. 13C3-CART and 13G2-CART specifically killed Tn+ COSMC-KO HaCaTs, but not Tn- HaCaTs at 10 to 1 ratio of T cells to HaCaTs (FIG 6). Referring to Table 17, the time to kill 50% COSMC-KO HaCaTs was 7.3 hrs for 13C3-CART and 8.75 for 13G2-CART. The data suggests 13C3-CART and 13G2-CART selectively target LAMP1-Tn.

Table 17: Time to kill 50% of cells (KT50)					
Target Cell	T Cell ratio	3C7 (KT50)	13C3 (KT50)	13G2 (KT50)	T cells (KT50)
HaCAT COSMC-KO	10:1	N/A	7.3 hrs	8.75 hrs	N/A

N/A = 50% of cells were not killed.

6.6 Example 6: Sequence Analysis of Anti-Glyco-LAMP1 Antibodies

[0433] Rapid Amplification of cDNA Ends (RACE) was performed to determine the heavy chain and light chain nucleotide sequences for 3C7, 13C3, and 13G2. The nucleotide sequences encoding the heavy and light chain variable regions of 3C7 are set forth in SEQ ID NO:21 and SEQ ID NO:22, respectively. The heavy and light chain variable regions encoded by SEQ ID NO:21 and SEQ ID NO:22 are set forth in SEQ ID NO:1 and SEQ ID NO:2, respectively. The predicted heavy chain CDR sequences (IMGT definition) are set forth in SEQ ID NOS:3-5, respectively, and the predicted light chain CDR sequences (IMGT definition) are set forth in SEQ ID NOS:6-8, respectively. The predicted heavy chain CDR sequences (Kabat definition) are set forth in SEQ ID NO:9-11, respectively, and the predicted light chain CDR sequences (Kabat definition) are set forth in SEQ ID NO:12-14, respectively. The predicted heavy chain CDR sequences (Chothia definition) are set forth in SEQ ID NO:15-17, respectively, and the predicted light chain CDR sequences (Chothia definition) are set forth in SEQ ID NO:18-20, respectively.

[0434] The nucleotide sequences encoding the heavy and light chain variable regions of 13C3 are set forth in SEQ ID NO:43 and SEQ ID NO:44, respectively. The heavy and light chain variable regions encoded by SEQ ID NO:43 and SEQ ID NO:44 are set forth in SEQ ID NO:23 and SEQ ID NO:24, respectively. The predicted heavy chain CDR sequences (IMGT definition) are set forth in SEQ ID NOS:25-27, respectively, and the predicted light chain CDR sequences (IMGT definition) are set forth in SEQ ID NOS:28-30, respectively. The predicted heavy chain CDR sequences (Kabat definition) are set forth in SEQ ID NOS:31-33, respectively, and the predicted light chain CDR sequences (Kabat definition) are set forth in SEQ ID NOS:34-36, respectively. The predicted heavy chain CDR sequences (Chothia definition) are set forth in SEQ ID NOS:37-39, respectively, and the predicted light chain CDR sequences (Chothia definition) are set forth in SEQ ID NOS:40-42, respectively.

[0435] The nucleotide sequences encoding the heavy and light chain variable regions of 13G2 are set forth in SEQ ID NO:65 and SEQ ID NO: 66, respectively. The heavy and light chain variable regions encoded by SEQ ID NO:65 and SEQ ID NO: 66 are set forth in SEQ ID NO:45 and SEQ ID NO: 46, respectively. The predicted heavy chain CDR sequences (IMGT definition) are set forth in SEQ ID NOS:47-49, respectively, and the predicted light chain CDR sequences (IMGT definition) are set forth in SEQ ID NOS:50-52, respectively. The predicted heavy chain CDR sequences (Kabat definition) are set forth in SEQ ID NOS:53-55, respectively, and the predicted light chain CDR sequences (Kabat definition) are set forth in SEQ ID NOS:56-58, respectively. The predicted heavy chain CDR sequences (Chothia definition) are set forth in SEQ ID NOS:59-61, respectively, and the predicted light chain CDR sequences (Chothia definition) are set forth in SEQ ID NOS:62-64, respectively.

6.7 Example 7: Tn-LAMP1 based ADCs

6.7.1. Overview

[0436] Antibody drug conjugates (ADCs) covalently attached to 3C7.2C11.1C9, 13C3.1C8.1C9, and 13G2.1A10.2G5 were produced. LAMP1-ADCs were then evaluated in target-specific cytotoxicity assay.

6.7.2. Materials and Methods

6.7.2.1 ADC production

[0437] ADCs were created by covalently attaching MC-GGFG-DX8951 to 3C7.2C11.1C9, 13C3.1C8.1C9, and 13G2.1A10.2G5. Drug antibody ratios (DARs) were calculated by mass spectrometry. The DARs for 13c3 was 3.1 and 13G2 was 5.6. The DAR could not be calculated for 3C7-ADC (Table 15).

6.7.3. Results

[0438] 3C7-ADC (GGFG-DX8951), 13C3-ADC (GGFG-DX8951) and 13G2-ADC (GGFG-DX8951) specifically killed Tn+ COSMC-KO T47Ds, but not Tn- T47D or Tn- HaCaTs (FIG. 5A-

1 to 5A-3). Referring to Table 18 the IC₅₀ for cell death was 4.5 nM for 3C7-ADC, 5.6 nM for 13C3-ADC, and 5.6 nM for 13G2-ADC.

Table 18: IC ₅₀ of Antibody drug conjugates (ADCs)			
ADC	DAR	T47D COSMC-KO Cells (EC ₅₀)	T47D cells (EC ₅₀)
GO-3C7	?	4.5 nM	504 nM
GO-13C3	~3.1	5.6 nM	205 nM
GO13G2	~5.6	5.6 nM	4.40 nM

6.8 Example 8: Humanized Antibodies

6.8.1. Overview

[0439] The murine antibody 13C3 was humanized using standard CDR-grafting technology. For the heavy chain, four templates, IGHV3-72*01, IGHV3-23*05, IGHV7-4-1*02, and IGHV3 were employed in order to generate CDR-grafted versions containing successively aggressive levels of humanization, *i.e.*, identity to the human acceptor germline. Similarly for the light chain, three templates, IGKV2-30*02, IGKV4-1*01, and IGKV7-3*01, were employed to generate CDR-grafted versions containing successively aggressive levels of humanization.

[0440] Expression constructs were designed for expression in Expi-293 cells. IL2 secretion signals were added to both heavy and light chain constructs. Antibodies were purified with ProteinA beads using conventional methods. Humanized candidates were evaluated for their ability to binding to the non-glycosylated and Tn-glycosylated LAMP1 peptides using ELISA. The humanized candidates were also compared to the parental antibody by size exclusion chromatography and Octet to determine binding affinity to the peptide antigen.

6.8.2. Materials and Methods

6.8.2.1 Vector Design

[0441] For each germline, three humanize versions were created: a conservative “A” sequence, a less conservative “B” sequence, and an “aggressive” “C” sequence (see Tables 4A-4G). Consensus sequences of all three of the A, B, and C sequences for each germline were also created that reflect the most common amino acid residue at each position.

[0442] These humanized templates were assembled and assayed for optimal biophysical and functional properties in two phases. In the first phase, up to 12 pairs of the conservative “A” designs were constructed and assayed for binding to the LAMP1 glycopeptide. After selection

of the most optimal combination based upon the “A” designs, the conservative “A” designs were iteratively replaced with the less conservative “B” designs and ultimately with the least conservative “C” designs.

6.8.2.2 ELISA

[0443] 96-well Corning high bind ELISA microplates plates were coated with LAMP1 peptides titrated in 0.2 M bicarbonate buffer, pH 9.4 overnight at 4 °C in concentrations ranging from 0.08 µg/ml to 10 µg/ml. BSA was used as a control/measure of background. The plates were then blocked with SuperBlock™ (Thermo Fisher) for 1 hr at room temperature. After plate washing, the humanized variants of 13C3 were incubated on the ELISA plate for 1 hour. All tested variants were expressed and purified using conventional methods. Briefly, Expi-293 cells were transiently transfected with heavy and light chain constructs, antibodies were secreted into supernatant and purified using Protein A agarose beads. The plates were then washed, and then incubated with secondary antibody (1/3000 Goat Anti-mouse IgG (H+L) HRP (Abcam 62-6520)) for 1 hour. The plate was then washed and color was developed with 1-Step™ Ultra TMB (Thermo Fisher) for 2 minutes. Color development was then stopped with 2 N Sulfuric Acid. Absorbance at 450 nm was then measured.

6.8.2.3 Bio-Layer Interferometry (Octet)

[0444] Antibody affinity of the humanized candidates of 13C3 can be assessed against specific antigens using BLI. In a BLI assay, the antigen can be immobilized onto a biosensor (e.g., the LAMP1-Tn peptide -CEQDRPSPTTAPPAPPSPSP (the amino acid portion of which is SEQ ID NO: 154) or a negative control analyte such as an unglycosylated LAMP1 peptide (Biotin-CEQDRPSPTTAPPAPPSPSP (the amino acid portion of which is SEQ ID NO: 155)) and presented to one antibody candidate for affinity measurements or two competing antibodies in tandem (or consecutive steps) for epitope binning. The binding to non-overlapping epitopes occurs if saturation with the first antibody does not block the binding of the second antibody. The affinity is determined by fitting the binding curve to a specific model: a 1:1 monovalent model or a 2:1 bivalent model. The error (>95% confidence) is calculated by how close the generated curve matches the model.

6.8.2.4 Size Exclusion Chromatography

[0445] The humanized candidates for 13C3 were tested for the presence of soluble protein aggregates using size exclusion chromatography (SEC). Briefly, purified antibodies were loaded on an HPLC silica TSK-GEL G3000SW column (TOSOH Biosciences, Montgomeryville, PA) and associated UV detector (166 Detector). The mobile phase composition was PBS and flow rate was 1.0 mL/min. Concentrations of protein species were determined by monitoring the absorbance of column eluate at 280 nm.

6.8.3. Results

[0446] Antibody drug conjugates (ADCs) covalently attached to humanized 13C3 were produced. The drug conjugate was covalently linked to cleavable MMAE with maleimide (vc-PAB-MMAE). ADCs were created by covalently attaching cleavable MMAE with maleimide (vc-PAB-MMAE) to 13C3. Drug antibody ratios (DARs) were calculated by mass spectrometry. Measurements were taken by Octet and ELISA for affinity to synthetic antigen (LAMP1-GP). Aggregation of the purified antibodies was quantified by Size Exclusion Chromatography (SEC).

[0447] The characteristics of the humanized ADCs are summarized in Table 19.

Table 19: Summary of characteristics of humanized LAMP1 candidates									
S.NO	Molecules	Humanization		Octet		SEC		ELISA	
		% Identity		LAMP1-GP		Peak area%		LAMP1-GP (EC50 ng/ml)	
		HC	LC	Rank	Affinity	Rank	Main peak	Rank	Affinity
1	13C3-HV-23-A/13C3 KV2-A	80%	90%	3	3.3	1	100	2	17.734
2	13C3-HV-72-A/13C3 KV2-A	84%	90%	2	3.1	4	98.01	5	26.16
3	13C3-HV-23-B/13C3 KV2-A	83%	90%	1	0.85	2	99.56	3	19.07
4	13C3-HV-72-B/13C3 KV2-A	87%	90%	4	8.2	3	99.42	4	25.75
5	13C3-HV-23-C/13C3 KV2-A	85%	90%	5	23.5	5	98.86	1	15.47
6	13C3 chimera				3.2 nM		98.62	-	18.4

[0448] Two of the humanized ADCs were further characterized in a target-specific cytotoxicity assay: humanized GO-13C3-Human-v1 (HV-72A/KV2A) and GO-13C3-Human-v2 (HV23B/KV2A). Referring to FIG. 5B and Table 20 the IC50 for cell death was 5.03 nM for 13C3 Human-v1, and 5.4 nM for 13C3 Human-v2.

Table 20: IC50 of Antibody drug conjugates (ADCs)			
ADC	DAR	T47D COSMC-KO Cells (EC50)	T47D cells (EC50)
GO-13C3 mouse	~4	4.5 nM	>100 uM
GO-13C3 Human-v1	~4	5.03 nM	>100 uM
GO-13C3 Human-v2	~4	5.4 nM	>100 uM

6.9 Example 9: *In vivo* activity of LAMP-ADC in CDx solid tumor mouse model

[0449] A CDx T47D (COSMC-KO) solid tumor model was established by flank injection. The tumor volume at CART injection was 100 mm³. Mice were treated with cleavable13C3-vc-PAB-MMAE (DAR = ~4) by IP injection (5 doses at 2.5mg/Kg or 5 mg/Kg) . Tumor volume was measured by caliper, treatment resulted in approximately 58% inhibition of tumor growth (FIG. 7). No clinical signs indicating adverse events was observed in treated mice.

7. SPECIFIC EMBODIMENTS, CITATION OF REFERENCES

[0450] While various specific embodiments have been illustrated and described, it will be appreciated that various changes can be made without departing from the spirit and scope of the disclosure(s). The present disclosure is exemplified by the numbered embodiments set forth below.

1. An anti-glyco-LAMP1 antibody or antigen binding fragment that specifically binds to, or specifically competes for binding to:

- (a) a LAMP1 peptide comprising CEQDRPSP**IT**APPAPPSPSP (SEQ ID NO:200) or a fragment thereof that has been glycosylated with GalNAc on the threonine residue shown with bold and underlined text ("the first LAMP1 glycopeptide");
- (b) a LAMP1 peptide comprising CEQDRPSP**IT**APPAPPSPSP (SEQ ID NO:216) or a fragment thereof that has been glycosylated with GalNAc on the threonine residues shown with bold and underlined text ("the second LAMP1 glycopeptide");
- (c) a LAMP1 peptide comprising CEQDRP**SP****IT**APPAPPSPSP (SEQ ID NO:217) or a fragment thereof that has been glycosylated with GalNAc on the serine and threonine residues shown with bold and underlined text ("the third LAMP1 glycopeptide"); or
- (d) a LAMP1 peptide comprising CEQDRP**SP****IT**APPAPPSPSP (SEQ ID NO:154) or a fragment thereof that has been glycosylated with GalNAc on the serine and threonine residues shown with bold and underlined text ("the fourth LAMP1 glycopeptide").

2. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 1 which specifically binds to, or specifically competes for binding to, the first LAMP1 glycopeptide.

3. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 1 which specifically binds to, or specifically competes for binding to, the second LAMP1 glycopeptide.

4. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 1 which specifically binds to, or specifically competes for binding to, the third LAMP1 glycopeptide.

5. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 1 which specifically binds to, or specifically competes for binding to, the fourth LAMP1 glycopeptide.

6. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of embodiments 1 to 5, wherein the fragment of the first LAMP1 glycopeptide, the second LAMP1 glycopeptide, the third LAMP1 glycopeptide, or the fourth LAMP1 glycopeptide comprises amino acids 5-11, 5-12, 5-13, 5-14, 5-15, 5-16, 5-17, 5-18, 5-19, or 5-20 of SEQ ID NO:200, 216, 217, or 154, respectively.

7. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of embodiments 1 to 5, wherein the fragment of the first LAMP1 glycopeptide, the second LAMP1 glycopeptide, the third LAMP1 glycopeptide, or the fourth LAMP1 glycopeptide comprises amino acids 4-11, 4-12, 4-13, 4-14, 4-15, 4-16, 4-17, 4-18, 4-19, or 4-20 of SEQ ID NO:200, 216, 217, or 154, respectively.

8. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of embodiments 1 to 5, wherein the fragment of the first LAMP1 glycopeptide, the second LAMP1 glycopeptide, the third LAMP1 glycopeptide, or the fourth LAMP1 glycopeptide comprises amino acids 3-11, 3-12, 3-13, 3-14, 3-15, 3-16, 3-17, 3-18, 3-19, or 3-20 of SEQ ID NO:200, 216, 217, or 154, respectively.

9. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of embodiments 1 to 5, wherein the fragment of the first LAMP1 glycopeptide, the second LAMP1 glycopeptide, the third LAMP1 glycopeptide, or the fourth LAMP1 glycopeptide comprises amino acids 2-11, 2-12, 2-13, 2-14, 2-15, 2-16, 2-17, 2-18, 2-19, or 2-20 of SEQ ID NO:200, 216, 217, or 154, respectively.

10. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of embodiments 1 to 5, wherein the fragment of the first LAMP1 glycopeptide, the second LAMP1 glycopeptide, the third LAMP1 glycopeptide, or the fourth LAMP1 glycopeptide comprises amino acids 1-11, 1-12, 1-13, 1-14, 1-15, 1-16, 1-17, 1-18, 1-19, or 1-20 of SEQ ID NO:200, 216, 217, or 154, respectively.

11. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of embodiments 1 to 5, wherein the first LAMP1 glycopeptide, the second LAMP1 glycopeptide, the third LAMP1 glycopeptide, or the fourth LAMP1 glycopeptide comprises SEQ ID NO:200, 216, 217, or 154, respectively.

12. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of embodiments 1 to 5, wherein the first LAMP1 glycopeptide, the second LAMP1 glycopeptide, the third LAMP1 glycopeptide, or the fourth LAMP1 glycopeptide consists of SEQ ID NO:200, 216, 217, or 154, respectively.

13. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of embodiments 1 to 12, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment

competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of

EVKLEESGGGLVQPGGSMKVSCGASGFTFSDAWMDWVRQSPEKGLEWVAEMRSKAFNHAI
YYAESVKGRFTISRDDSKSRVYLQMNLLRPEDTGIYYCTPNWDEGFAYWGQGTTLTVSA

(SEQ ID NO:1) and a light chain variable (VL) sequence of

DVMLTQTPLSLPVSLGDQASISCRSSQSLVHSNGNTYLHWYLQKPGQSPKLLINKVSNRFFGV
PDRFSGSGSGTDFTLKISRVEAEDLGVYFCSQSTHVPRTFGGGTKLEIK (SEQ ID NO:2) for

binding to any one of the LAMP1 glycopeptides.

14. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of embodiments 1 to 12, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of

EVKLEDSGGGLVQPGGSMKLSCAASGFTFSDAWMDWVRHSPEKGLEWVAELRSKAFNHAT
YYAESVKGRFTISRDDSKSTVYLQMNSLRAEDTGIYYCTPNWDEGFAYWGQGTTLTVSA

(SEQ ID NO:23) and a light chain variable (VL) sequence of

DVVMQTPLSLPVSLGDQASISCRSSQSLVHSNGNTYLHWYLQKPGQSPKLLINKVSNRFSGV
PDRFSGSGSGTDFTLKISRVEAEDLGVYFCSQSTHVPRTFGGGTKLEIK (SEQ ID NO:24) for

binding to any one of the LAMP1 glycopeptides.

15. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of embodiments 1 to 12, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of

EVRLEESGGGLVQPGGSMKLSCVASGFTFSDAWMDWVRQSPERGLEWVAELRSKTFNHAT
YYAESVRGRFTISRDDSKSTVYLQMNSLRAEDTGIYYCSPNWDEGFAYWGQGTTLTVSA

(SEQ ID NO:45) and a light chain variable (VL) sequence of

DVVMTQIPLSLCVSLGDQASISCRSSQSLVHNNGNTYLHWYLQKPGQSPKLLINKVSKRFTGV
PDRFSGSGSGTDFTLKISRVEAEDLGVYFCSQSTHVPRTFGGGTKLEIK (SEQ ID NO:46) for

binding to any one of the LAMP1 glycopeptides.

16. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of embodiments 1 to 12, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of

EVQLLES GGGLVQPGGSLRLSCAASGFTFSDAWMDWVRHAPGKGLEWVAELRSKAFNHATY
YAESVKGRFTISRDDSKNTVYLQMNSLRAEDTAVYYCTPNWDEGFAYWGQGTTLTVSS (SEQ

ID NO:133) and a light chain variable (VL) sequence of

DVVMTQSPLSLPVTLGQPASISCRSSQSLVHSNGNTYLHWYQQRPGQSPRLLINKVSNRFSG
VPDRFSGSGSGTDFTLKISRVEAEDVGVYFCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:145)

for binding to any one of the LAMP1 glycopeptides.

17. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of embodiments 1 to 12, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of

EVQLLES GGGGLVQP GGSRLS CAASGFTFSDAWMDWVRHAPGKGLEWVAELRSKAFNHATY
YAESVKGRFTISRDDSKNTVYLQMNSLRAEDTAVYYCTPNWDEGFAYWGQGTLVTVSS (SEQ
ID NO:133) and a light chain variable (VL) sequence of
DVVMTQSPLSLPVTLGQPASISCRSSQSLVHSNGNTYLHWFQQRPGQSPRLLINKVSNRFSG
VPDRFSGSGSGTDFTLKISRVEAEDVGVYYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:146)
for binding to any one of the LAMP1 glycopeptides.

18. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of embodiments 1 to 12, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of

EVQLLES GGGGLVQP GGSRLS CAASGFTFSDAWMDWVRHAPGKGLEWVAELRSKAFNHATY
YAESVKGRFTISRDDSKNTVYLQMNSLRAEDTAVYYCTPNWDEGFAYWGQGTLVTVSS (SEQ
ID NO:133) and a light chain variable (VL) sequence of
DVVMTQSPLSLPVTLGQPASISCRSSQSLVHSNANVYLHWFQQRPGQSPRLLINKVSNRFSGV
PDRFSGSGSGTDFTLKISRVEAEDVGVYYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:147) for
binding to any one of the LAMP1 glycopeptides.

19. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of embodiments 1 to 12, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of

EVQLLES GGGGLVQP GGSRLS CAASGFTFSDAWMDWVRHAPGKGLEWVAELRSKAFNHATY
YAESVKGRFTISRDDSKNTVYLQMNSLRAEDTAVYYCTPNWDEGFAYWGQGTLVTVSS (SEQ
ID NO:133) and a light chain variable (VL) sequence of
DVVMTQSPDSLAVSLGERATINCRSSQSLVHSNGNTYLHWYQQKPGQPPKLLINKVSNRFSG
VPDRFSGSGSGTDFTLTISLQAEDVAVYFCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:148)
for binding to any one of the LAMP1 glycopeptides.

20. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of embodiments 1 to 10, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of

EVQLLES GGGGLVQP GGSRLS CAASGFTFSDAWMDWVRHAPGKGLEWVAELRSKAFNHATY
YAESVKGRFTISRDDSKNTVYLQMNSLRAEDTAVYYCTPNWDEGFAYWGQGTLVTVSS (SEQ
ID NO:133) and a light chain variable (VL) sequence of
DVVMTQSPDSLAVSLGERATINCKSSQSLLSHNGNTYLHWYQQKPGQPPKLLINKVSTRFSGV

PDRFSGSGSGTDFTLTISLQAEDVAVYYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:149) for binding to any one of the LAMP1 glycopeptides.

21. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of embodiments 1 to 10, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of

EVQLLES GGGLVQP GGSLRLSCAASGFTFSDAWMDWVRHAPGKGLEWVAELRSKAFNHATY
YAESVKGRFTISRDDSKNTVYLQMNSLRAEDTAVYYCTPNWDEGFAYWGQGLTVTVSS (SEQ
ID NO:133) and a light chain variable (VL) sequence of

DVVMTQSPDSLAVSLGERATINCKSSQSLLSNANVYLHWYQQKPGQPPKLLINKASTRESGV
PDRFSGSGSGTDFTLTISLQAEDVAVYYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:150) for
binding to any one of the LAMP1 glycopeptides.

22. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of embodiments 1 to 10, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of

EVQLLES GGGLVQP GGSLRLSCAASGFTFSDAWMDWVRHAPGKGLEWVAELRSKAFNHATY
YAESVKGRFTISRDDSKNTVYLQMNSLRAEDTAVYYCTPNWDEGFAYWGQGLTVTVSS (SEQ
ID NO:133) and a light chain variable (VL) sequence of

DVVMTQSPASLAVSPGQRATITCRSSQSLVHSNGNTYLHWYQQKPGQPPKLLINKVSNRFSG
VPARFSGSGSGTDFTLTINPVEANDTANYFCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:151)
for binding to any one of the LAMP1 glycopeptides.

23. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of embodiments 1 to 10, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of

EVQLLES GGGLVQP GGSLRLSCAASGFTFSDAWMDWVRHAPGKGLEWVAELRSKAFNHATY
YAESVKGRFTISRDDSKNTVYLQMNSLRAEDTAVYYCTPNWDEGFAYWGQGLTVTVSS (SEQ
ID NO:133) and a light chain variable (VL) sequence of

DVVLTSQSPASLAVSPGQRATITCRSSQSLVHSNGNTYLHWYQQKPGQPPKLLINKVSNKFTGV
PARFSGSGSGTDFTLTINPVEANDTANYFCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:152) for
binding to any one of the LAMP1 glycopeptides.

24. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of embodiments 1 to 10, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of

EVQLLES GGGLVQP GGSLRLSCAASGFTFSDAWMDWVRHAPGKGLEWVAELRSKAFNHATY
YAESVKGRFTISRDDSKNTVYLQMNSLRAEDTAVYYCTPNWDEGFAYWGQGLTVTVSS (SEQ

ID NO:133) and a light chain variable (VL) sequence of DVVLTQSPASLAVSPGQRATITCRASELSHSNANVYIHWWYQQKPGQPPKLLINKASNKFTGV PARFSGSGSGTDFTLTINPVEANDTANYCYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:153) for binding to any one of the LAMP1 glycopeptides.

25. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of embodiments 1 to 10, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of

EVQLLESQGGGLVQPGGSLRLSCAASGFTFSDAWMDWVRQAPGKGLEWVSELRSKAFNHATY YAESVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCTPNWDEGFAYWGQGTLVTVSS (SEQ ID NO:134) and a light chain variable (VL) sequence of DVVMTQSPSLPVTLGQPASISCRSSQSLVHSNGNTYLHWYQQRPGQSPRLLINKVSNRFSG VPDRFSGSGSGTDFTLKISRVEAEDVGVYFCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:145) for binding to any one of the LAMP1 glycopeptides.

26. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of embodiments 1 to 10, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of

EVQLLESQGGGLVQPGGSLRLSCAASGFTFSDAWMDWVRQAPGKGLEWVSELRSKAFNHATY YAESVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCTPNWDEGFAYWGQGTLVTVSS (SEQ ID NO:134) and a light chain variable (VL) sequence of DVVMTQSPSLPVTLGQPASISCRSSQSLVHSNGNTYLHWFQQRPGQSPRLLINKVSNRFSG VPDRFSGSGSGTDFTLKISRVEAEDVGVYYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:146) for binding to any one of the LAMP1 glycopeptides.

27. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of embodiments 1 to 10, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of

EVQLLESQGGGLVQPGGSLRLSCAASGFTFSDAWMDWVRQAPGKGLEWVSELRSKAFNHATY YAESVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCTPNWDEGFAYWGQGTLVTVSS (SEQ ID NO:134) and a light chain variable (VL) sequence of DVVMTQSPSLPVTLGQPASISCRSSQSLVHSNANVYLHWFQQRPGQSPRLLINKVSNRFSGV PDRFSGSGSGTDFTLKISRVEAEDVGVYYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:147) for binding to any one of the LAMP1 glycopeptides.

28. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of embodiments 1 to 10, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of

EVQLLESGGGLVQPGGSLRLSCAASGFTFSDAWMDWVRQAPGKGLEWVSELRSKAFNHATY
 YAESVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCTPNWDEGFAYWGQGTLVTVSS (SEQ
 ID NO:134) and a light chain variable (VL) sequence of
 DVVMTQSPDSLAVSLGERATINCRSSQSLVHSNGNTYLHWYQQKPGQPPKLLINKVSNRFSG
 VPDRFSGSGSGTDFTLTISLQAEDVAVYFCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:148)
 for binding to any one of the LAMP1 glycopeptides.

29. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of
 embodiments 1 to 10, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment
 competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH)
 sequence of

EVQLLESGGGLVQPGGSLRLSCAASGFTFSDAWMDWVRQAPGKGLEWVSELRSKAFNHATY
 YAESVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCTPNWDEGFAYWGQGTLVTVSS (SEQ
 ID NO:134) and a light chain variable (VL) sequence of
 DVVMTQSPDSLAVSLGERATINCKSSQSLHNSNGNTYLHWYQQKPGQPPKLLINKVSTRFSGV
 PDRFSGSGSGTDFTLTISLQAEDVAVYYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:149) for
 binding to any one of the LAMP1 glycopeptides.

30. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of
 embodiments 1 to 10, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment
 competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH)
 sequence of

EVQLLESGGGLVQPGGSLRLSCAASGFTFSDAWMDWVRQAPGKGLEWVSELRSKAFNHATY
 YAESVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCTPNWDEGFAYWGQGTLVTVSS (SEQ
 ID NO:134) and a light chain variable (VL) sequence of
 DVVMTQSPDSLAVSLGERATINCKSSQSLHNSNANVYLHWYQQKPGQPPKLLINKASTRESGV
 PDRFSGSGSGTDFTLTISLQAEDVAVYYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:150) for
 binding to any one of the LAMP1 glycopeptides.

31. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of
 embodiments 1 to 10, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment
 competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH)
 sequence of

EVQLLESGGGLVQPGGSLRLSCAASGFTFSDAWMDWVRQAPGKGLEWVSELRSKAFNHATY
 YAESVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCTPNWDEGFAYWGQGTLVTVSS (SEQ
 ID NO:134) and a light chain variable (VL) sequence of
 DVVMTQSPASLAVSPGQRATITCRSSQSLVHSNGNTYLHWYQQKPGQPPKLLINKVSNRFSG
 VPARFSGSGSGTDFTLTINPVEANDTANYFCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:151)
 for binding to any one of the LAMP1 glycopeptides.

32. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of
 embodiments 1 to 10, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment

competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of

EVQLLESGGGLVQPGGSLRLSCAASGFTFSDAWMDWVRQAPGKGLEWVSELRSKAFNHATY
YAESVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCTPNWDEGFAYWGQGTLVTVSS (SEQ
ID NO:134) and a light chain variable (VL) sequence of
DVVLTSQSPASLAVSPGQRATITCRSSESLSHSNGNTYLHWYQQKPGQPPKLLINKVSNKFTGV
PARFSGSGSGTDFTLTINPVEANDTANYCYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:152) for
binding to any one of the LAMP1 glycopeptides.

33. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of
embodiments 1 to 10, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment
competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH)
sequence of

EVQLLESGGGLVQPGGSLRLSCAASGFTFSDAWMDWVRQAPGKGLEWVSELRSKAFNHATY
YAESVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCTPNWDEGFAYWGQGTLVTVSS (SEQ
ID NO:134) and a light chain variable (VL) sequence of
DVVLTSQSPASLAVSPGQRATITCRASESLSHSNANVYIHWYQQKPGQPPKLLINKASNKFTGV
PARFSGSGSGTDFTLTINPVEANDTANYCYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:153) for
binding to any one of the LAMP1 glycopeptides.

34. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of
embodiments 1 to 10, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment
competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH)
sequence of

EVQLLESGGGLVQPGGSLRLSCAASGFTFSDAWMDWVRQAPGKGLEWVSEIRSSAFNHATY
YAESVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCTPNWDEGFAYWGQGTLVTVSS (SEQ
ID NO:135) and a light chain variable (VL) sequence of
DVVMTQSPLSLPVTLGQPASISCRSSQSLVHSNGNTYLHWYQQRPQGQSPRLLINKVSNRFSG
VPDRFSGSGSGTDFTLKISRVEAEDVGVYFCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:145)
for binding to any one of the LAMP1 glycopeptides.

35. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of
embodiments 1 to 10, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment
competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH)
sequence of

EVQLLESGGGLVQPGGSLRLSCAASGFTFSDAWMDWVRQAPGKGLEWVSEIRSSAFNHATY
YAESVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCTPNWDEGFAYWGQGTLVTVSS (SEQ
ID NO:135) and a light chain variable (VL) sequence of
DVVMTQSPLSLPVTLGQPASISCRSSQSLVHSNGNTYLHWFQQRPQGQSPRLLINKVSNRFSG
VPDRFSGSGSGTDFTLKISRVEAEDVGVYCYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:146)
for binding to any one of the LAMP1 glycopeptides.

36. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of embodiments 1 to 10, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of

EVQLLES GGGGLVQP GGSRLS CAASGFTFSDAWMDWVRQAPGKGLEWVSEIRSSAFNHATY
YAESVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCTPNWDEGFAYWGQGTLVTVSS (SEQ
ID NO:135) and a light chain variable (VL) sequence of

DVVMTQSPSLPVTLGQPASISCRSSQSLVHSNANVYLHWYFQQRPQGQSPRLLINKVSNRFGV
PDRFSGSGSGTDFTLKISRVEAEDVGVYYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:147) for
binding to any one of the LAMP1 glycopeptides.

37. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of embodiments 1 to 10, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of

EVQLLES GGGGLVQP GGSRLS CAASGFTFSDAWMDWVRQAPGKGLEWVSEIRSSAFNHATY
YAESVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCTPNWDEGFAYWGQGTLVTVSS (SEQ
ID NO:135) and a light chain variable (VL) sequence of

DVVMTQSPDSLAVSLGERATINCRSSQSLVHSNGNTYLHWYQQKPGQPPKLLINKVSNRFG
VPDRFSGSGSGTDFTLTISLQAEDVAVYFCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:148)
for binding to any one of the LAMP1 glycopeptides.

38. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of embodiments 1 to 10, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of

EVQLLES GGGGLVQP GGSRLS CAASGFTFSDAWMDWVRQAPGKGLEWVSEIRSSAFNHATY
YAESVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCTPNWDEGFAYWGQGTLVTVSS (SEQ
ID NO:135) and a light chain variable (VL) sequence of

DVVMTQSPDSLAVSLGERATINCKSSQSLLSHNGNTYLHWYQQKPGQPPKLLINKVSTRFGV
PDRFSGSGSGTDFTLTISLQAEDVAVYYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:149) for
binding to any one of the LAMP1 glycopeptides.

39. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of embodiments 1 to 10, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of

EVQLLES GGGGLVQP GGSRLS CAASGFTFSDAWMDWVRQAPGKGLEWVSEIRSSAFNHATY
YAESVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCTPNWDEGFAYWGQGTLVTVSS (SEQ
ID NO:135) and a light chain variable (VL) sequence of

DVVMTQSPDSLAVSLGERATINCKSSQSLLSHNGNTYLHWYQQKPGQPPKLLINKASTRESGV

PDRFSGSGSGTDFTLTISLQAEDVAVYYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:150) for binding to any one of the LAMP1 glycopeptides.

40. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of embodiments 1 to 10, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of

EVQLLES GGGLVQP GGSLRLSCAASGFTFSDAWMDWVRQAPGKGLEWVSEIRSSAFNHATY
YAESVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCTPNWDEGFAYWGQGTLVTVSS (SEQ
ID NO:135) and a light chain variable (VL) sequence of

DVVMTQSPASLAVSPGQRATITCRSSQSLVHSNGNTYLHWYQQKPGQPPKLLINKVSNRFSG
VPAFSGSGSGTDFTLTINPVEANDTANYFCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:151)
for binding to any one of the LAMP1 glycopeptides.

41. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of embodiments 1 to 10, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of

EVQLLES GGGLVQP GGSLRLSCAASGFTFSDAWMDWVRQAPGKGLEWVSEIRSSAFNHATY
YAESVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCTPNWDEGFAYWGQGTLVTVSS (SEQ
ID NO:135) and a light chain variable (VL) sequence of

DVVLTSQSPASLAVSPGQRATITCRSSESLSHSNGNTYLHWYQQKPGQPPKLLINKVSNKFTGV
PARFSGSGSGTDFTLTINPVEANDTANYYYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:152) for
binding to any one of the LAMP1 glycopeptides.

42. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of embodiments 1 to 10, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of

EVQLLES GGGLVQP GGSLRLSCAASGFTFSDAWMDWVRQAPGKGLEWVSEIRSSAFNHATY
YAESVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCTPNWDEGFAYWGQGTLVTVSS (SEQ
ID NO:135) and a light chain variable (VL) sequence of

DVVLTSQSPASLAVSPGQRATITCRASELSHSNANVYIHWYQQKPGQPPKLLINKASNKFTGV
PARFSGSGSGTDFTLTINPVEANDTANYYYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:153) for
binding to any one of the LAMP1 glycopeptides.

43. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 1, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of

EVQLVES GGGLVKP GGSLRLSCAASGFTFSDAWMDWVRHAPGKGLEWVAELRSKAFNHATY
YAESVKGRFTISRDDSKNTVYLQMNSLKTEDTAVYYCTPNWDEGFAYWGQGTLVTVSS (SEQ
ID NO:136) and a light chain variable (VL) sequence of

DVVMTQSPLSLPVTLGQPASISCRSSQSLVHSNGNTYLHWYQQRPGQSPRLLINKVSNRFSG
VPDRFSGSGSGTDFTLKISRVEAEDVGVYFCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:145)
for binding to any one of the LAMP1 glycopeptides.

44. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of
embodiments 1 to 10, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment
competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH)
sequence of

EVQLVESGGGLVKPGGSLRLSCAASGFTFSDAWMDWVRHAPGKGLEWVAELRSKAFNHATY
YAESVKGRFTISRDDSKNTVYLQMNSLKTEDTAVYYCTPNWDEGFAYWGQGTLVTVSS (SEQ
ID NO:136) and a light chain variable (VL) sequence of
DVVMTQSPLSLPVTLGQPASISCRSSQSLVHSNGNTYLHWFQQRPGQSPRLLINKVSNRFSG
VPDRFSGSGSGTDFTLKISRVEAEDVGVYFCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:146)
for binding to any one of the LAMP1 glycopeptides.

45. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of
embodiments 1 to 10, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment
competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH)
sequence of

EVQLVESGGGLVKPGGSLRLSCAASGFTFSDAWMDWVRHAPGKGLEWVAELRSKAFNHATY
YAESVKGRFTISRDDSKNTVYLQMNSLKTEDTAVYYCTPNWDEGFAYWGQGTLVTVSS (SEQ
ID NO:136) and a light chain variable (VL) sequence of
DVVMTQSPLSLPVTLGQPASISCRSSQSLVHSNANVYLHWFQQRPGQSPRLLINKVSNRFSGV
PDRFSGSGSGTDFTLKISRVEAEDVGVYFCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:147) for
binding to any one of the LAMP1 glycopeptides.

46. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of
embodiments 1 to 10, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment
competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH)
sequence of

EVQLVESGGGLVKPGGSLRLSCAASGFTFSDAWMDWVRHAPGKGLEWVAELRSKAFNHATY
YAESVKGRFTISRDDSKNTVYLQMNSLKTEDTAVYYCTPNWDEGFAYWGQGTLVTVSS (SEQ
ID NO:136) and a light chain variable (VL) sequence of
DVVMTQSPDSLAVSLGERATINCRSSQSLVHSNGNTYLHWYQKPGQPPKLLINKVSNRFSG
VPDRFSGSGSGTDFTLTISLQAEDVAVYFCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:148)
for binding to any one of the LAMP1 glycopeptides.

47. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of
embodiments 1 to 10, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment
competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH)
sequence of

EVQLVESGGGLVKPGGSLRLSCAASGFTFSDAWMDWVRHAPGKGLEWVAELRSKAFNHATY

YAESVKGRFTISRDDSKNTVYLQMNSLKTEDTAVYYCTPNWDEGFAYWGQGLTVTVSS (SEQ ID NO:136) and a light chain variable (VL) sequence of DVVMTQSPDSLAVSLGERATINCKSSQSLLSNNGNTYLHWYQQKPGQPPKLLINKVSTRFSGV PDRFSGSGSGTDFTLTISLQAEDVAVYYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:149) for binding to any one of the LAMP1 glycopeptides.

48. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of embodiments 1 to 10, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of

EVQLVESGGGLVKPGGSLRLSCAASGFTFSDAWMDWVRHAPGKGLEWVAELRSKAFNHATY YAESVKGRFTISRDDSKNTVYLQMNSLKTEDTAVYYCTPNWDEGFAYWGQGLTVTVSS (SEQ ID NO:136) and a light chain variable (VL) sequence of DVVMTQSPDSLAVSLGERATINCKSSQSLLSNANVYLHWYQQKPGQPPKLLINKASTRESGV PDRFSGSGSGTDFTLTISLQAEDVAVYYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:150) for binding to any one of the LAMP1 glycopeptides.

49. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of embodiments 1 to 10, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of

EVQLVESGGGLVKPGGSLRLSCAASGFTFSDAWMDWVRHAPGKGLEWVAELRSKAFNHATY YAESVKGRFTISRDDSKNTVYLQMNSLKTEDTAVYYCTPNWDEGFAYWGQGLTVTVSS (SEQ ID NO:136) and a light chain variable (VL) sequence of DVVMTQSPASLAVSPGQRATITCRSSQSLVHSNNGNTYLHWYQQKPGQPPKLLINKVSNRFSG VPARFSGSGSGTDFTLTINPVEANDTANYFCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:151) for binding to any one of the LAMP1 glycopeptides.

50. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of embodiments 1 to 10, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of

EVQLVESGGGLVKPGGSLRLSCAASGFTFSDAWMDWVRHAPGKGLEWVAELRSKAFNHATY YAESVKGRFTISRDDSKNTVYLQMNSLKTEDTAVYYCTPNWDEGFAYWGQGLTVTVSS (SEQ ID NO:136) and a light chain variable (VL) sequence of DVVLTQSPASLAVSPGQRATITCRSSQSLVHSNNGNTYLHWYQQKPGQPPKLLINKVSNKFTGV PARFSGSGSGTDFTLTINPVEANDTANYFCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:152) for binding to any one of the LAMP1 glycopeptides.

51. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of embodiments 1 to 10, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH)

sequence of

EVQLVESGGGLVKPGGSLRLSCAASGFTFSDAWMDWVRHAPGKGLEWVAELRSKAFNHATY
YAESVKGRFTISRDDSKNTVYLQMNSLKTEDTAVYYCTPNWDEGFAYWGQGTLVTVSS (SEQ
ID NO:136) and a light chain variable (VL) sequence of
DVVLTQSPASLAVSPGQRATITCRASESLSHSNANVYIHWYQQKPGQPPKLLINKASNKFTGV
PARFSGSGSGTDFTLTINPVEANDTANYCYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:153) for
binding to any one of the LAMP1 glycopeptides.

52. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of
embodiments 1 to 10, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment
competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH)
sequence of

EVQLVESGGGLVKPGGSLRLSCAASGFTFSDAWMDWVRQAPGKGLEWVGELRSKAFNHAT
YYAESVKGRFTISRDDSKNTLYLQMNSLKTEDTAVYYCTPNWDEGFAYWGQGTLVTVSS
(SEQ ID NO:137) and a light chain variable (VL) sequence of
DVVMTQSPLSLPVTLGQPASISCRSSQSLVHSNGNTYLHWYQQRPGQSPRLLINKVSNRFSG
VPDRFSGSGSGTDFTLKISRVEAEDVGVYFCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:145)
for binding to any one of the LAMP1 glycopeptides.

53. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of
embodiments 1 to 10, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment
competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH)
sequence of

EVQLVESGGGLVKPGGSLRLSCAASGFTFSDAWMDWVRQAPGKGLEWVGELRSKAFNHAT
YYAESVKGRFTISRDDSKNTLYLQMNSLKTEDTAVYYCTPNWDEGFAYWGQGTLVTVSS
(SEQ ID NO:137) and a light chain variable (VL) sequence of
DVVMTQSPLSLPVTLGQPASISCRSSQSLVHSNGNTYLHWFQQRPGQSPRLLINKVSNRFSG
VPDRFSGSGSGTDFTLKISRVEAEDVGVYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:146)
for binding to any one of the LAMP1 glycopeptides.

54. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of
embodiments 1 to 10, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment
competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH)
sequence of

EVQLVESGGGLVKPGGSLRLSCAASGFTFSDAWMDWVRQAPGKGLEWVGELRSKAFNHAT
YYAESVKGRFTISRDDSKNTLYLQMNSLKTEDTAVYYCTPNWDEGFAYWGQGTLVTVSS
(SEQ ID NO:137) and a light chain variable (VL) sequence of
DVVMTQSPLSLPVTLGQPASISCRSSQSLVHSNANVYLHWFQQRPGQSPRLLINKVSNRFSGV
PDRFSGSGSGTDFTLKISRVEAEDVGVYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:147) for
binding to any one of the LAMP1 glycopeptides.

55. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of embodiments 1 to 10, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of

EVQLVESGGGLVKGPGSLRLSCAASGFTFSDAWMDWVRQAPGKGLEWVGELRSKAFNHAT
YYAESVKGRFTISRDDSKNTLYLQMNSLKTEDTAVYYCTPNWDEGFAYWGQGTLTVSS

(SEQ ID NO:137) and a light chain variable (VL) sequence of

DVVMTQSPDSLAVSLGERATINCRSSQSLVHSNGNTYLHWYQQKPGQPPKLLINKVSNRFSG
VPDRFSGSGSGTDFTLTISLQAEDVAVYFCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:148)

for binding to any one of the LAMP1 glycopeptides.

56. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of embodiments 1 to 10, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of

EVQLVESGGGLVKGPGSLRLSCAASGFTFSDAWMDWVRQAPGKGLEWVGELRSKAFNHAT
YYAESVKGRFTISRDDSKNTLYLQMNSLKTEDTAVYYCTPNWDEGFAYWGQGTLTVSS

(SEQ ID NO:137) and a light chain variable (VL) sequence of

DVVMTQSPDSLAVSLGERATINCKSSQSLHNSNGNTYLHWYQQKPGQPPKLLINKVSTRFSGV
PDRFSGSGSGTDFTLTISLQAEDVAVYYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:149) for

binding to any one of the LAMP1 glycopeptides.

57. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of embodiments 1 to 10, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of

EVQLVESGGGLVKGPGSLRLSCAASGFTFSDAWMDWVRQAPGKGLEWVGELRSKAFNHAT
YYAESVKGRFTISRDDSKNTLYLQMNSLKTEDTAVYYCTPNWDEGFAYWGQGTLTVSS

(SEQ ID NO:137) and a light chain variable (VL) sequence of

DVVMTQSPDSLAVSLGERATINCKSSQSLHNSNANVYLHWYQQKPGQPPKLLINKASTRESGV
PDRFSGSGSGTDFTLTISLQAEDVAVYYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:150) for

binding to any one of the LAMP1 glycopeptides.

58. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of embodiments 1 to 10, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of

EVQLVESGGGLVKGPGSLRLSCAASGFTFSDAWMDWVRQAPGKGLEWVGELRSKAFNHAT
YYAESVKGRFTISRDDSKNTLYLQMNSLKTEDTAVYYCTPNWDEGFAYWGQGTLTVSS

(SEQ ID NO:137) and a light chain variable (VL) sequence of

DVVMTQSPASLAVSPGQRATITCRSSQSLVHSNGNTYLHWYQQKPGQPPKLLINKVSNRFSG

VPARFSGSGSGTDFTLTINPVEANDTANYFCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:151) for binding to any one of the LAMP1 glycopeptides.

59. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of embodiments 1 to 10, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of

EVQLVESGGGLVKPGGSLRLSCAASGFTFSDAWMDWVRQAPGKGLEWVGELRSKAFNHAT
YYAESVKGRFTISRDDSKNTLYLQMNSLKTEDTAVYYCTPNWDEGFAYWGQGTLLTVSS

(SEQ ID NO:137) and a light chain variable (VL) sequence of

DVVLTSQSPASLAVSPGQRATITCRSSESLSHSNGNTYLHWYQQKPGQPPKLLINKVSNKFTGV
PARFSGSGSGTDFTLTINPVEANDTANYCYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:152) for

binding to any one of the LAMP1 glycopeptides.

60. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of embodiments 1 to 10, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of

EVQLVESGGGLVKPGGSLRLSCAASGFTFSDAWMDWVRQAPGKGLEWVGELRSKAFNHAT
YYAESVKGRFTISRDDSKNTLYLQMNSLKTEDTAVYYCTPNWDEGFAYWGQGTLLTVSS

(SEQ ID NO:137) and a light chain variable (VL) sequence of

DVVLTSQSPASLAVSPGQRATITCRASESLSHSNANVYIHWYQQKPGQPPKLLINKASNKFTGV
PARFSGSGSGTDFTLTINPVEANDTANYCYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:153) for

binding to any one of the LAMP1 glycopeptides.

61. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of embodiments 1 to 10, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of

EVQLVESGGGLVKPGGSLRLSCAASGFTFSDAWMDWVRQAPGKGLEWVGELRSKAFNHATY
YAEPVKGRFTISRDDSKNTLYLQMNSLKTEDTAVYYCTPNWDEGFAYWGQGTLLTVSS (SEQ

ID NO:138) and a light chain variable (VL) sequence of

DVVMTSQSPSLPVTLGQPASISCRSSQSLVHSNGNTYLHWYQQRPQGQSPRLLINKVSNRFSG
VPDRFSGSGSGTDFTLTKISRVEAEDVGVYFCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:145)

for binding to any one of the LAMP1 glycopeptides.

62. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of embodiments 1 to 10, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of

EVQLVESGGGLVKPGGSLRLSCAASGFTFSDAWMDWVRQAPGKGLEWVGELRSKAFNHATY
YAEPVKGRFTISRDDSKNTLYLQMNSLKTEDTAVYYCTPNWDEGFAYWGQGTLLTVSS (SEQ

ID NO:138) and a light chain variable (VL) sequence of
 DVVMTQSPLSLPVTLGQPASISCRSSQSLVHSNGNTYLHWFFQQRPGQSPRLLINKVSNRFSG
 VPDRFSGSGSGTDFTLKISRVEAEDVGVYYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:146)
 for binding to any one of the LAMP1 glycopeptides.

63. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of
 embodiments 1 to 10, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment
 competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH)
 sequence of

EVQLVESGGGLVKPGGSLRLSCAASGFTFSDAWMDWVRQAPGKGLEWVGEIRSKAFNHATY
 YAEPVKGRFTISRDDSKNTLYLQMNSLKTEDTAVYYCTPNWDEGFAYWGQGTLLTVSS (SEQ
 ID NO:138) and a light chain variable (VL) sequence of
 DVVMTQSPLSLPVTLGQPASISCRSSQSLVHSNANVYLHWFFQQRPGQSPRLLINKVSNRFSGV
 PDRFSGSGSGTDFTLKISRVEAEDVGVYYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:147) for
 binding to any one of the LAMP1 glycopeptides.

64. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of
 embodiments 1 to 10, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment
 competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH)
 sequence of

EVQLVESGGGLVKPGGSLRLSCAASGFTFSDAWMDWVRQAPGKGLEWVGEIRSKAFNHATY
 YAEPVKGRFTISRDDSKNTLYLQMNSLKTEDTAVYYCTPNWDEGFAYWGQGTLLTVSS (SEQ
 ID NO:138) and a light chain variable (VL) sequence of
 DVVMTQSPDSLAVSLGERATINCRSSQSLVHSNGNTYLHWYQQKPGQPPKLLINKVSNRFSG
 VPDRFSGSGSGTDFTLTISLQAEDVAVYFCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:148)
 for binding to any one of the LAMP1 glycopeptides.

65. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of
 embodiments 1 to 10, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment
 competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH)
 sequence of

EVQLVESGGGLVKPGGSLRLSCAASGFTFSDAWMDWVRQAPGKGLEWVGEIRSKAFNHATY
 YAEPVKGRFTISRDDSKNTLYLQMNSLKTEDTAVYYCTPNWDEGFAYWGQGTLLTVSS (SEQ
 ID NO:138) and a light chain variable (VL) sequence of
 DVVMTQSPDSLAVSLGERATINCKSSQSLHSNGNTYLHWYQQKPGQPPKLLINKVSTRFSGV
 PDRFSGSGSGTDFTLTISLQAEDVAVYYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:149) for
 binding to any one of the LAMP1 glycopeptides.

66. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of
 embodiments 1 to 10, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment
 competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH)
 sequence of

EVQLVESGGGLVKPGGSLRLSCAASGFTFSDAWMDWVRQAPGKGLEWVGEIRSKAFNHATY
YAEPVKGRFTISRDDSKNTLYLQMNSLKTEDTAVYYCTPNWDEGFAYWGQGTLLTVSS (SEQ
ID NO:138) and a light chain variable (VL) sequence of
DVVMTQSPDSLAVSLGERATINCKSSQSLLSNANVYLHWYQQKPGQPPKLLINKASTRESGV
PDRFSGSGSGTDFTLTISLQAEDVAVYYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:150) for
binding to any one of the LAMP1 glycopeptides.

67. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of
embodiments 1 to 10, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment
competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH)
sequence of

EVQLVESGGGLVKPGGSLRLSCAASGFTFSDAWMDWVRQAPGKGLEWVGEIRSKAFNHATY
YAEPVKGRFTISRDDSKNTLYLQMNSLKTEDTAVYYCTPNWDEGFAYWGQGTLLTVSS (SEQ
ID NO:138) and a light chain variable (VL) sequence of
DVVMTQSPASLAVSPGQRATITCRSSQSLVHSNGNTYLHWYQQKPGQPPKLLINKVSNRFSG
VPAFSGSGSGTDFTLTINPVEANDTANYFCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:151)
for binding to any one of the LAMP1 glycopeptides.

68. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of
embodiments 1 to 10, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment
competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH)
sequence of

EVQLVESGGGLVKPGGSLRLSCAASGFTFSDAWMDWVRQAPGKGLEWVGEIRSKAFNHATY
YAEPVKGRFTISRDDSKNTLYLQMNSLKTEDTAVYYCTPNWDEGFAYWGQGTLLTVSS (SEQ
ID NO:138) and a light chain variable (VL) sequence of
DVVLTQSPASLAVSPGQRATITCRSSQSLVHSNGNTYLHWYQQKPGQPPKLLINKVSNKFTGV
PARFSGSGSGTDFTLTINPVEANDTANYFCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:152) for
binding to any one of the LAMP1 glycopeptides.

69. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of
embodiments 1 to 10, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment
competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH)
sequence of

EVQLVESGGGLVKPGGSLRLSCAASGFTFSDAWMDWVRQAPGKGLEWVGEIRSKAFNHATY
YAEPVKGRFTISRDDSKNTLYLQMNSLKTEDTAVYYCTPNWDEGFAYWGQGTLLTVSS (SEQ
ID NO:138) and a light chain variable (VL) sequence of
DVVLTQSPASLAVSPGQRATITCRASELSHSNANVYIHWYQQKPGQPPKLLINKASNKFTGV
PARFSGSGSGTDFTLTINPVEANDTANYFCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:153) for
binding to any one of the LAMP1 glycopeptides.

70. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of
embodiments 1 to 10, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment

competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of

EVQLVESGGGLVQPGGSLRLSCAASGFTFSDAWMDWVRHAPGKGLEWVAELRSKAFNHATY
YAESVKGRFTISRDDSKNSVYLQMNSLKTEDTAVYYCTPNWDEGFAYWGQGTLVTVSS (SEQ
ID NO:139) and a light chain variable (VL) sequence of

DVVMTQSPLSLPVTLGQPASISCRSSQSLVHSNGNTYLHWYQQRPGQSPRLLINKVSNRFSG
VPDRFSGSGSGTDFTLKISRVEAEDVGVYFCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:145)
for binding to any one of the LAMP1 glycopeptides.

71. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of
embodiments 1 to 10, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment
competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH)
sequence of

EVQLVESGGGLVQPGGSLRLSCAASGFTFSDAWMDWVRHAPGKGLEWVAELRSKAFNHATY
YAESVKGRFTISRDDSKNSVYLQMNSLKTEDTAVYYCTPNWDEGFAYWGQGTLVTVSS (SEQ
ID NO:139) and a light chain variable (VL) sequence of

DVVMTQSPLSLPVTLGQPASISCRSSQSLVHSNGNTYLHWFQQRPGQSPRLLINKVSNRFSG
VPDRFSGSGSGTDFTLKISRVEAEDVGVYYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:146)
for binding to any one of the LAMP1 glycopeptides.

72. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of
embodiments 1 to 10, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment
competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH)
sequence of

EVQLVESGGGLVQPGGSLRLSCAASGFTFSDAWMDWVRHAPGKGLEWVAELRSKAFNHATY
YAESVKGRFTISRDDSKNSVYLQMNSLKTEDTAVYYCTPNWDEGFAYWGQGTLVTVSS (SEQ
ID NO:139) and a light chain variable (VL) sequence of

DVVMTQSPLSLPVTLGQPASISCRSSQSLVHSNANVYLHWFQQRPGQSPRLLINKVSNRFSGV
PDRFSGSGSGTDFTLKISRVEAEDVGVYYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:147) for
binding to any one of the LAMP1 glycopeptides.

73. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of
embodiments 1 to 10, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment
competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH)
sequence of

EVQLVESGGGLVQPGGSLRLSCAASGFTFSDAWMDWVRHAPGKGLEWVAELRSKAFNHATY
YAESVKGRFTISRDDSKNSVYLQMNSLKTEDTAVYYCTPNWDEGFAYWGQGTLVTVSS (SEQ
ID NO:139) and a light chain variable (VL) sequence of

DVVMTQSPDSLAVSLGERATINCRSSQSLVHSNGNTYLHWYQQKPGQPPKLLINKVSNRFSG
VPDRFSGSGSGTDFTLTISLQAEDVAVYFCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:148)
for binding to any one of the LAMP1 glycopeptides.

74. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of embodiments 1 to 10, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of

EVQLVESGGGLVQPGGSLRLSCAASGFTFSDAWMDWVRHAPGKGLEWVAELRSKAFNHATY
YAESVKGRFTISRDDSKNSVYLQMNSLKTEDTAVYYCTPNWDEGFAYWGQGTLVTVSS (SEQ
ID NO:139) and a light chain variable (VL) sequence of
DVVMTQSPDSLAVSLGERATINCKSSQSLLSHNGNTYLHWYQQKPGQPPKLLINKVSTRFSGV
PDRFSGSGSGTDFTLTISLQAEDVAVYYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:149) for
binding to any one of the LAMP1 glycopeptides.

75. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of embodiments 1 to 10, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of

EVQLVESGGGLVQPGGSLRLSCAASGFTFSDAWMDWVRHAPGKGLEWVAELRSKAFNHATY
YAESVKGRFTISRDDSKNSVYLQMNSLKTEDTAVYYCTPNWDEGFAYWGQGTLVTVSS (SEQ
ID NO:139) and a light chain variable (VL) sequence of
DVVMTQSPDSLAVSLGERATINCKSSQSLLSHNGNTYLHWYQQKPGQPPKLLINKASTRESGV
PDRFSGSGSGTDFTLTISLQAEDVAVYYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:150) for
binding to any one of the LAMP1 glycopeptides.

76. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of embodiments 1 to 10, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of

EVQLVESGGGLVQPGGSLRLSCAASGFTFSDAWMDWVRHAPGKGLEWVAELRSKAFNHATY
YAESVKGRFTISRDDSKNSVYLQMNSLKTEDTAVYYCTPNWDEGFAYWGQGTLVTVSS (SEQ
ID NO:139) and a light chain variable (VL) sequence of
DVVMTQSPASLAVSPGQRATITCRSSQSLVSHNGNTYLHWYQQKPGQPPKLLINKVSNRFSG
VPAFSGSGSGTDFTLTINPVEANDTANYFCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:151)
for binding to any one of the LAMP1 glycopeptides.

77. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of embodiments 1 to 10, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of

EVQLVESGGGLVQPGGSLRLSCAASGFTFSDAWMDWVRHAPGKGLEWVAELRSKAFNHATY
YAESVKGRFTISRDDSKNSVYLQMNSLKTEDTAVYYCTPNWDEGFAYWGQGTLVTVSS (SEQ
ID NO:139) and a light chain variable (VL) sequence of
DVVLTQSPASLAVSPGQRATITCRSSESLSHSNGNTYLHWYQQKPGQPPKLLINKVSNKFTGV

PARFSGSGSGTDFLTINPVEANDTANYCYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:152) for binding to any one of the LAMP1 glycopeptides.

78. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of embodiments 1 to 10, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of

EVQLVESGGGLVQPGGSLRLSCAASGFTFSDAWMDWVRHAPGKGLEWVAELRSKAFNHATY
YAESVKGRFTISRDDSKNSVYLQMNSLKTEDTAVYYCTPNWDEGFAYWGQGTLVTVSS (SEQ
ID NO:139) and a light chain variable (VL) sequence of

DVVLTSQSPASLAVSPGQRATITCRASELSHSNANVYIHWHYQQKPGQPPKLLINKASNKFTGV
PARFSGSGSGTDFLTINPVEANDTANYCYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:153) for binding to any one of the LAMP1 glycopeptides.

79. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of embodiments 1 to 10, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of

EVQLVESGGGLVQPGGSLRLSCAASGFTFSDAWMDWVRQAPGKGLEWVGELRSKAFNHAT
YYAESVKGRFTISRDDSKNSLYLQMNSLKTEDTAVYYCTPNWDEGFAYWGQGTLVTVSS
(SEQ ID NO:140) and a light chain variable (VL) sequence of

DVVMTSQSPSLPVTLGQPASISCRSSQSLVHSNGNTYLHWYQQRPQGQSPRLLINKVSNRFSG
VPDRFSGSGSGTDFTLKISRVEAEDVGVYFCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:145)
for binding to any one of the LAMP1 glycopeptides.

80. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of embodiments 1 to 10, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of

EVQLVESGGGLVQPGGSLRLSCAASGFTFSDAWMDWVRQAPGKGLEWVGELRSKAFNHAT
YYAESVKGRFTISRDDSKNSLYLQMNSLKTEDTAVYYCTPNWDEGFAYWGQGTLVTVSS
(SEQ ID NO:140) and a light chain variable (VL) sequence of

DVVMTSQSPSLPVTLGQPASISCRSSQSLVHSNGNTYLHWFQQRPQGQSPRLLINKVSNRFSG
VPDRFSGSGSGTDFTLKISRVEAEDVGVYCYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:146)
for binding to any one of the LAMP1 glycopeptides.

81. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of embodiments 1 to 10, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of

EVQLVESGGGLVQPGGSLRLSCAASGFTFSDAWMDWVRQAPGKGLEWVGELRSKAFNHAT
YYAESVKGRFTISRDDSKNSLYLQMNSLKTEDTAVYYCTPNWDEGFAYWGQGTLVTVSS

(SEQ ID NO:140) and a light chain variable (VL) sequence of DVVMTQSPLSLPVTLGQPASISCRSSQSLVHSNANVYLHWYQQKPGQSPRLLINKVSNRFGV PDRFSGSGSGTDFTLKISRVEAEDVGVYYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:147) for binding to any one of the LAMP1 glycopeptides.

82. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of embodiments 1 to 10, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of

EVQLVESGGGLVQPGGSLRLSCAASGFTFSDAWMDWVRQAPGKGLEWVGELRSKAFNHAT YYAESVKGRFTISRDDSKNSLYLQMNSLKTEDTAVYYCTPNWDEGFAYWGQGTLVTVSS

(SEQ ID NO:140) and a light chain variable (VL) sequence of DVVMTQSPDSLAVSLGERATINCRSSQSLVHSNGNTYLHWYQQKPGQPPKLLINKVSNRFGV VPDRFSGSGSGTDFTLTISLQAEDVAVYFCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:148) for binding to any one of the LAMP1 glycopeptides.

83. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of embodiments 1 to 10, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of

EVQLVESGGGLVQPGGSLRLSCAASGFTFSDAWMDWVRQAPGKGLEWVGELRSKAFNHAT YYAESVKGRFTISRDDSKNSLYLQMNSLKTEDTAVYYCTPNWDEGFAYWGQGTLVTVSS

(SEQ ID NO:140) and a light chain variable (VL) sequence of DVVMTQSPDSLAVSLGERATINCKSSQSLHNSNGNTYLHWYQQKPGQPPKLLINKVSTRFGV PDRFSGSGSGTDFTLTISLQAEDVAVYYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:149) for binding to any one of the LAMP1 glycopeptides.

84. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of embodiments 1 to 10, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of

EVQLVESGGGLVQPGGSLRLSCAASGFTFSDAWMDWVRQAPGKGLEWVGELRSKAFNHAT YYAESVKGRFTISRDDSKNSLYLQMNSLKTEDTAVYYCTPNWDEGFAYWGQGTLVTVSS

(SEQ ID NO:140) and a light chain variable (VL) sequence of DVVMTQSPDSLAVSLGERATINCKSSQSLHNSNANVYLHWYQQKPGQPPKLLINKASTRESGV PDRFSGSGSGTDFTLTISLQAEDVAVYYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:150) for binding to any one of the LAMP1 glycopeptides.

85. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of embodiments 1 to 10, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of

EVQLVESGGGLVQPGGSLRLSCAASGFTFSDAWMDWVRQAPGKGLEWVGELRSKAFNHAT
YYAESVKGRFTISRDDSKNSLYLQMNSLKTEDTAVYYCTPNWDEGFAYWGQGTLVTVSS
(SEQ ID NO:140) and a light chain variable (VL) sequence of
DVVMTQSPASLAVSPGQRATITCRSSQSLVHSNGNTYLHWYQQKPGQPPKLLINKVSNRFSG
VPARFSGSGSGTDFTLTINPVEANDTANYFCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:151)
for binding to any one of the LAMP1 glycopeptides.

86. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of
embodiments 1 to 10, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment
competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH)
sequence of

EVQLVESGGGLVQPGGSLRLSCAASGFTFSDAWMDWVRQAPGKGLEWVGELRSKAFNHAT
YYAESVKGRFTISRDDSKNSLYLQMNSLKTEDTAVYYCTPNWDEGFAYWGQGTLVTVSS
(SEQ ID NO:140) and a light chain variable (VL) sequence of
DVVLTQSPASLAVSPGQRATITCRSSESLSHSNGNTYLHWYQQKPGQPPKLLINKVSNKFTGV
PARFSGSGSGTDFTLTINPVEANDTANYCYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:152) for
binding to any one of the LAMP1 glycopeptides.

87. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of
embodiments 1 to 10, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment
competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH)
sequence of

EVQLVESGGGLVQPGGSLRLSCAASGFTFSDAWMDWVRQAPGKGLEWVGELRSKAFNHAT
YYAESVKGRFTISRDDSKNSLYLQMNSLKTEDTAVYYCTPNWDEGFAYWGQGTLVTVSS
(SEQ ID NO:140) and a light chain variable (VL) sequence of
DVVLTQSPASLAVSPGQRATITCRASESLSHSNANVYIHWYQQKPGQPPKLLINKASNKFTGV
PARFSGSGSGTDFTLTINPVEANDTANYCYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:153) for
binding to any one of the LAMP1 glycopeptides.

88. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of
embodiments 1 to 10, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment
competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH)
sequence of

EVQLVESGGGLVQPGGSLRLSCAASGFTFSDAWMDWVRQAPGKGLEWVGETRASKAFNYAT
YYAESVKGRFTISRDDSKNSLYLQMNSLKTEDTAVYYCTPNWDEGFAYWGQGTLVTVSS
(SEQ ID NO:141) and a light chain variable (VL) sequence of
DVVMTQSPLSLPVTLGQPASISCRSSQSLVHSNGNTYLHWYQQRPGQSPRLLINKVSNRFSG
VPDRFSGSGSGTDFTLKISRVEAEDVGVYFCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:145)
for binding to any one of the LAMP1 glycopeptides.

89. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of
embodiments 1 to 10, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment

competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of

EVQLVESGGGLVQPGGSLRLSCAASGFTFSDAWMDWVRQAPGKGLEWVGETRSKAFNYAT
YYAESVKGRFTISRDDSKNSLYLQMNSLKTEDTAVYYCTPNWDEGFAYWGQGTLVTVSS

(SEQ ID NO:141) and a light chain variable (VL) sequence of

DVVMTQSPLSLPVTLGQPASISCRSSQSLVHSNGNTYLHWFQQRPGQSPRLLINKVSNRFSG
VPDRFSGSGSGTDFTLKISRVEAEDVGVYYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:146)

for binding to any one of the LAMP1 glycopeptides.

90. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of embodiments 1 to 10, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of

EVQLVESGGGLVQPGGSLRLSCAASGFTFSDAWMDWVRQAPGKGLEWVGETRSKAFNYAT
YYAESVKGRFTISRDDSKNSLYLQMNSLKTEDTAVYYCTPNWDEGFAYWGQGTLVTVSS

(SEQ ID NO:141) and a light chain variable (VL) sequence of

DVVMTQSPLSLPVTLGQPASISCRSSQSLVHSNANVYLHWFQQRPGQSPRLLINKVSNRFSGV
PDRFSGSGSGTDFTLKISRVEAEDVGVYYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:147) for

binding to any one of the LAMP1 glycopeptides.

91. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of embodiments 1 to 10, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of

EVQLVESGGGLVQPGGSLRLSCAASGFTFSDAWMDWVRQAPGKGLEWVGETRSKAFNYAT
YYAESVKGRFTISRDDSKNSLYLQMNSLKTEDTAVYYCTPNWDEGFAYWGQGTLVTVSS

(SEQ ID NO:141) and a light chain variable (VL) sequence of

DVVMTQSPDSLAVSLGERATINCRSSQSLVHSNGNTYLHWYQQKPGQPPKLLINKVSNRFSG
VPDRFSGSGSGTDFTLTISLQAEDVAVYFCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:148)

for binding to any one of the LAMP1 glycopeptides.

92. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of embodiments 1 to 10, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of

EVQLVESGGGLVQPGGSLRLSCAASGFTFSDAWMDWVRQAPGKGLEWVGETRSKAFNYAT
YYAESVKGRFTISRDDSKNSLYLQMNSLKTEDTAVYYCTPNWDEGFAYWGQGTLVTVSS

(SEQ ID NO:141) and a light chain variable (VL) sequence of

DVVMTQSPDSLAVSLGERATINCKSSQSLHSNGNTYLHWYQQKPGQPPKLLINKVSTRFSGV
PDRFSGSGSGTDFTLTISLQAEDVAVYYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:149) for

binding to any one of the LAMP1 glycopeptides.

93. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of embodiments 1 to 10, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of

EVQLVESGGGLVQPGGSLRLSCAASGFTFSDAWMDWVRQAPGKGLEWVGETRSKAFNYAT
YYAESVKGRFTISRDDSKNSLYLQMNSLKTEDTAVYYCTPNWDEGFAYWGQGTLVTVSS
(SEQ ID NO:141) and a light chain variable (VL) sequence of

DVVMTQSPDSLAVSLGERATINCKSSQSLLSNANVYLHWYQQKPGQPPKLLINKASTRESGV
PDRFSGSGSGTDFTLTISLQAEDVAVYYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:150) for binding to any one of the LAMP1 glycopeptides.

94. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of embodiments 1 to 10, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of

EVQLVESGGGLVQPGGSLRLSCAASGFTFSDAWMDWVRQAPGKGLEWVGETRSKAFNYAT
YYAESVKGRFTISRDDSKNSLYLQMNSLKTEDTAVYYCTPNWDEGFAYWGQGTLVTVSS
(SEQ ID NO:141) and a light chain variable (VL) sequence of

DVVMTQSPASLAVSPGQRATITCRSSQSLVHSNGNTYLHWYQQKPGQPPKLLINKVSNRFSG
VPAFSGSGSGTDFTLTINPVEANDTANYFCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:151)
for binding to any one of the LAMP1 glycopeptides.

95. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of embodiments 1 to 10, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of

EVQLVESGGGLVQPGGSLRLSCAASGFTFSDAWMDWVRQAPGKGLEWVGETRSKAFNYAT
YYAESVKGRFTISRDDSKNSLYLQMNSLKTEDTAVYYCTPNWDEGFAYWGQGTLVTVSS
(SEQ ID NO:141) and a light chain variable (VL) sequence of

DVVLTSQSPASLAVSPGQRATITCRSSESLSHSNGNTYLHWYQQKPGQPPKLLINKVSNKFTGV
PARFSGSGSGTDFTLTINPVEANDTANYYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:152) for binding to any one of the LAMP1 glycopeptides.

96. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of embodiments 1 to 10, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of

EVQLVESGGGLVQPGGSLRLSCAASGFTFSDAWMDWVRQAPGKGLEWVGETRSKAFNYAT
YYAESVKGRFTISRDDSKNSLYLQMNSLKTEDTAVYYCTPNWDEGFAYWGQGTLVTVSS
(SEQ ID NO:141) and a light chain variable (VL) sequence of

DVVLTSQSPASLAVSPGQRATITCRASESLSHSNANVYIHWYQQKPGQPPKLLINKASNKFTGV

PARFSGSGSGTDFTLTINPVEANDTANYYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:153) for binding to any one of the LAMP1 glycopeptides.

97. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of embodiments 1 to 10, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of

QVQLVQSGSELKKPGASVKVSCASGFTFSDAWMDWVRHAPGQGLEWVAELRSKAFNHAT
YYAESVKGRFVISRDDSVSTVYLQISSLKAEDTAVYYCTPNWDEGFAYWGQGLTVTVSS (SEQ ID NO:142) and a light chain variable (VL) sequence of

DVVMTQSPLSLPVTLGQPASISCRSSQSLVHSNGNTYLHWYQQRPGQSPRLLINKVSNRFSG
VPDRFSGSGSGTDFTLKISRVEAEDVGVYFCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:145) for binding to any one of the LAMP1 glycopeptides.

98. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of embodiments 1 to 10, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of

QVQLVQSGSELKKPGASVKVSCASGFTFSDAWMDWVRHAPGQGLEWVAELRSKAFNHAT
YYAESVKGRFVISRDDSVSTVYLQISSLKAEDTAVYYCTPNWDEGFAYWGQGLTVTVSS (SEQ ID NO:142) and a light chain variable (VL) sequence of

DVVMTQSPLSLPVTLGQPASISCRSSQSLVHSNGNTYLHWFQQRPGQSPRLLINKVSNRFSG
VPDRFSGSGSGTDFTLKISRVEAEDVGVYYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:146) for binding to any one of the LAMP1 glycopeptides.

99. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of embodiments 1 to 10, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of

QVQLVQSGSELKKPGASVKVSCASGFTFSDAWMDWVRHAPGQGLEWVAELRSKAFNHAT
YYAESVKGRFVISRDDSVSTVYLQISSLKAEDTAVYYCTPNWDEGFAYWGQGLTVTVSS (SEQ ID NO:142) and a light chain variable (VL) sequence of

DVVMTQSPLSLPVTLGQPASISCRSSQSLVHSNANVYLHWFQQRPGQSPRLLINKVSNRFSGV
PDRFSGSGSGTDFTLKISRVEAEDVGVYYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:147) for binding to any one of the LAMP1 glycopeptides.

100. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of embodiments 1 to 10, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of

QVQLVQSGSELKKPGASVKVSCASGFTFSDAWMDWVRHAPGQGLEWVAELRSKAFNHAT
YYAESVKGRFVISRDDSVSTVYLQISSLKAEDTAVYYCTPNWDEGFAYWGQGLTVTVSS (SEQ

ID NO:142) and a light chain variable (VL) sequence of
 DVVMTQSPDSLAVSLGERATINCRSSQSLVHSNGNTYLHWYQQKPGQPPKLLINKVSNRFSG
 VPDRFSGSGSGTDFTLTISLQAEDVAVYFCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:148)
 for binding to any one of the LAMP1 glycopeptides.

101. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of
 embodiments 1 to 10, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment
 competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH)
 sequence of

QVQLVQSGSELKKPGASVKVSCASGFTFSDAWMDWVRHAPGQGLEWVAELRSKAFNHAT
 YYAESVKGRFVISRDDSSTVYLQISSLKAEDTAVYYCTPNWDEGFAYWGQGLTVTVSS (SEQ
 ID NO:142) and a light chain variable (VL) sequence of
 DVVMTQSPDSLAVSLGERATINCKSSQSLVHSNGNTYLHWYQQKPGQPPKLLINKVSTRFSGV
 PDRFSGSGSGTDFTLTISLQAEDVAVYYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:149) for
 binding to any one of the LAMP1 glycopeptides.

102. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of
 embodiments 1 to 10, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment
 competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH)
 sequence of

QVQLVQSGSELKKPGASVKVSCASGFTFSDAWMDWVRHAPGQGLEWVAELRSKAFNHAT
 YYAESVKGRFVISRDDSSTVYLQISSLKAEDTAVYYCTPNWDEGFAYWGQGLTVTVSS (SEQ
 ID NO:142) and a light chain variable (VL) sequence of
 DVVMTQSPDSLAVSLGERATINCKSSQSLVHSNANVYLHWYQQKPGQPPKLLINKASTRESGV
 PDRFSGSGSGTDFTLTISLQAEDVAVYYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:150) for
 binding to any one of the LAMP1 glycopeptides.

103. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of
 embodiments 1 to 10, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment
 competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH)
 sequence of

QVQLVQSGSELKKPGASVKVSCASGFTFSDAWMDWVRHAPGQGLEWVAELRSKAFNHAT
 YYAESVKGRFVISRDDSSTVYLQISSLKAEDTAVYYCTPNWDEGFAYWGQGLTVTVSS (SEQ
 ID NO:142) and a light chain variable (VL) sequence of
 DVVMTQSPASLAVSPGQRATITCRSSQSLVHSNGNTYLHWYQQKPGQPPKLLINKVSNRFSG
 VPARFSGSGSGTDFTLTINPVEANDTANYFCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:151)
 for binding to any one of the LAMP1 glycopeptides.

104. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of
 embodiments 1 to 10, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment
 competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH)
 sequence of

QVQLVQSGSELKKPGASVKVSCASGFTFSDAWMDWVRHAPGQGLEWVAELRSKAFNHAT
YYAESVKGRFVISRDDSVSTVYLQISSLKAEDTAVYYCTPNWDEGFAYWGQGLTVTVSS (SEQ
ID NO:142) and a light chain variable (VL) sequence of
DVVLTQSPASLAVSPGQRATITCRSSESLSHSNGNTYLHWYQQKPGQPPKLLINKVSNKFTGV
PARFSGSGSGTDFTLTINPVEANDTANYYYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:152) for
binding to any one of the LAMP1 glycopeptides.

105. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of
embodiments 1 to 10, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment
competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH)
sequence of

QVQLVQSGSELKKPGASVKVSCASGFTFSDAWMDWVRHAPGQGLEWVAELRSKAFNHAT
YYAESVKGRFVISRDDSVSTVYLQISSLKAEDTAVYYCTPNWDEGFAYWGQGLTVTVSS (SEQ
ID NO:142) and a light chain variable (VL) sequence of
DVVLTQSPASLAVSPGQRATITCRASESLSHSNANVYIHWYQQKPGQPPKLLINKASNKFTGV
PARFSGSGSGTDFTLTINPVEANDTANYYYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:153) for
binding to any one of the LAMP1 glycopeptides.

106. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of
embodiments 1 to 10, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment
competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH)
sequence of

QVQLVQSGSELKKPGASVKVSCASGYTFSDAWMDWVRQAPGQGLEWMGELRSKAFNHAT
YYAESVKGRFVISRDDSVSTAYLQISSLKAEDTAVYYCAPNWDEGFAYWGQGLTVTVSS (SEQ
ID NO:143) and a light chain variable (VL) sequence of
DVVMTQSPLSLPVTLGQPASISCRSSQSLVHSNGNTYLHWYQQRPGQSPRLLINKVSNRFSG
VPDRFSGSGSGTDFTLKISRVEAEDVGVYFCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:145)
for binding to any one of the LAMP1 glycopeptides.

107. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of
embodiments 1 to 10, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment
competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH)
sequence of

QVQLVQSGSELKKPGASVKVSCASGYTFSDAWMDWVRQAPGQGLEWMGELRSKAFNHAT
YYAESVKGRFVISRDDSVSTAYLQISSLKAEDTAVYYCAPNWDEGFAYWGQGLTVTVSS (SEQ
ID NO:143) and a light chain variable (VL) sequence of
DVVMTQSPLSLPVTLGQPASISCRSSQSLVHSNGNTYLHWFQQRPGQSPRLLINKVSNRFSG
VPDRFSGSGSGTDFTLKISRVEAEDVGVYYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:146)
for binding to any one of the LAMP1 glycopeptides.

108. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of
embodiments 1 to 10, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment

competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of

QVQLVQSGSELKKPGASVKVSCASGYTFSDAWMDWVRQAPGQGLEWMGELRSKAFNHAT
YYAESVKGRFVISRDDSVSTAYLQISSLKAEDTAVYYCAPNWDEGFAYWGQGTLVTVSS (SEQ
ID NO:143) and a light chain variable (VL) sequence of

DVVMTQSPSLPVTLGQPASISCRSSQSLVHSNANVYLHWYFQQRPQGQSPRLLINKVSNRFGV
PDRFSGSGSGTDFTLKISRVEAEDVGVYYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:147) for
binding to any one of the LAMP1 glycopeptides.

109. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of
embodiments 1 to 10, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment
competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH)
sequence of

QVQLVQSGSELKKPGASVKVSCASGYTFSDAWMDWVRQAPGQGLEWMGELRSKAFNHAT
YYAESVKGRFVISRDDSVSTAYLQISSLKAEDTAVYYCAPNWDEGFAYWGQGTLVTVSS (SEQ
ID NO:143) and a light chain variable (VL) sequence of

DVVMTQSPDSLAVSLGERATINCRSSQSLVHSNGNTYLHWYQQKPGQPPKLLINKVSNRFGV
VPDRFSGSGSGTDFTLTISLQAEDVAVYFCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:148)
for binding to any one of the LAMP1 glycopeptides.

110. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of
embodiments 1 to 10, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment
competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH)
sequence of

QVQLVQSGSELKKPGASVKVSCASGYTFSDAWMDWVRQAPGQGLEWMGELRSKAFNHAT
YYAESVKGRFVISRDDSVSTAYLQISSLKAEDTAVYYCAPNWDEGFAYWGQGTLVTVSS (SEQ
ID NO:143) and a light chain variable (VL) sequence of

DVVMTQSPDSLAVSLGERATINCKSSQSLHNSGNTYLHWYQQKPGQPPKLLINKVSTRFGV
PDRFSGSGSGTDFTLTISLQAEDVAVYYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:149) for
binding to any one of the LAMP1 glycopeptides.

111. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of
embodiments 1 to 10, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment
competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH)
sequence of

QVQLVQSGSELKKPGASVKVSCASGYTFSDAWMDWVRQAPGQGLEWMGELRSKAFNHAT
YYAESVKGRFVISRDDSVSTAYLQISSLKAEDTAVYYCAPNWDEGFAYWGQGTLVTVSS (SEQ
ID NO:143) and a light chain variable (VL) sequence of

DVVMTQSPDSLAVSLGERATINCKSSQSLHNSNANVYLHWYQQKPGQPPKLLINKASTRESGV
PDRFSGSGSGTDFTLTISLQAEDVAVYYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:150) for
binding to any one of the LAMP1 glycopeptides.

112. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of embodiments 1 to 10, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of

QVQLVQSGSELKKPGASVKVSCKASGYTFSDAWMDWVRQAPGQGLEWMGELRSKAFNHAT
YYAESVKGRFVISRDDSVSTAYLQISSLKAEDTAVYYCAPNWDEGFAYWGQGTLVTVSS (SEQ
ID NO:143) and a light chain variable (VL) sequence of
DVVMTQSPASLAVSPGQRATITCRSSQSLVHNSGNTYLHWYQQKPGQPPKLLINKVSNRFSG
VPARFSGSGSGTDFTLTINPVEANDTANYFCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:151)
for binding to any one of the LAMP1 glycopeptides.

113. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of embodiments 1 to 10, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of

QVQLVQSGSELKKPGASVKVSCKASGYTFSDAWMDWVRQAPGQGLEWMGELRSKAFNHAT
YYAESVKGRFVISRDDSVSTAYLQISSLKAEDTAVYYCAPNWDEGFAYWGQGTLVTVSS (SEQ
ID NO:143) and a light chain variable (VL) sequence of
DVVLTQSPASLAVSPGQRATITCRSSESLSHNSGNTYLHWYQQKPGQPPKLLINKVSNKFTGV
PARFSGSGSGTDFTLTINPVEANDTANYCYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:152) for
binding to any one of the LAMP1 glycopeptides.

114. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of embodiments 1 to 10, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of

QVQLVQSGSELKKPGASVKVSCKASGYTFSDAWMDWVRQAPGQGLEWMGELRSKAFNHAT
YYAESVKGRFVISRDDSVSTAYLQISSLKAEDTAVYYCAPNWDEGFAYWGQGTLVTVSS (SEQ
ID NO:143) and a light chain variable (VL) sequence of
DVVLTQSPASLAVSPGQRATITCRASESLSHSNANVYIHWYQQKPGQPPKLLINKASNKFTGV
PARFSGSGSGTDFTLTINPVEANDTANYCYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:153) for
binding to any one of the LAMP1 glycopeptides.

115. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of embodiments 1 to 10, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of

QVQLVQSGSELKKPGASVKVSCKASGYTFTSAWMNWVRQAPGQGLEWMGEIRTNFNAFHAP
YYAQGVKGRFVISRDDSVSTAYLQISSLKAEDTAVYYCAPNWDEGFAYWGQGTLVTVSS
(SEQ ID NO:144) and a light chain variable (VL) sequence of
DVVMTQSPLSLPVTLGQPASISCRSSQSLVHNSGNTYLHWYQQRPGQSPRLLINKVSNRFSG

VPDRFSGSGSGTDFTLKISRVEAEDVG VYFCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:145) for binding to any one of the LAMP1 glycopeptides.

116. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of embodiments 1 to 10, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of

QVQLVQSGSELKKPGASVKV SCKASGYTFTSAWMNWRQAPGQGLEWMGEIRTN A FNHAP
YYAQGVKGRFVISRDDSVSTAYLQISSLKAEDTAVYYCAPNWDEGFAYWGQGT LVT VSS

(SEQ ID NO:144) and a light chain variable (VL) sequence of

DVVM TQSPLSLPVT LGQPASISCRSSQSLVHSNGNTYLHWFQQRPGQSPRLLINKVSNRFSG
VPDRFSGSGSGTDFTLKISRVEAEDVG VYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:146)

for binding to any one of the LAMP1 glycopeptides.

117. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of embodiments 1 to 10, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of

QVQLVQSGSELKKPGASVKV SCKASGYTFTSAWMNWRQAPGQGLEWMGEIRTN A FNHAP
YYAQGVKGRFVISRDDSVSTAYLQISSLKAEDTAVYYCAPNWDEGFAYWGQGT LVT VSS

(SEQ ID NO:144) and a light chain variable (VL) sequence of

DVVM TQSPLSLPVT LGQPASISCRSSQSLVHSNANVYLHWFQQRPGQSPRLLINKVSNRFSGV
PDRFSGSGSGTDFTLKISRVEAEDVG VYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:147) for

binding to any one of the LAMP1 glycopeptides.

118. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of embodiments 1 to 10, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of

QVQLVQSGSELKKPGASVKV SCKASGYTFTSAWMNWRQAPGQGLEWMGEIRTN A FNHAP
YYAQGVKGRFVISRDDSVSTAYLQISSLKAEDTAVYYCAPNWDEGFAYWGQGT LVT VSS

(SEQ ID NO:144) and a light chain variable (VL) sequence of

DVVM TQSPDSLAVSLGERATINCRSSQSLVHSNGNTYLHWYQQKPGQPPKLLINKVSNRFSG
VPDRFSGSGSGTDFTLTISLQAEDVAVYFCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:148)

for binding to any one of the LAMP1 glycopeptides.

119. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of embodiments 1 to 10, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of

QVQLVQSGSELKKPGASVKV SCKASGYTFTSAWMNWRQAPGQGLEWMGEIRTN A FNHAP
YYAQGVKGRFVISRDDSVSTAYLQISSLKAEDTAVYYCAPNWDEGFAYWGQGT LVT VSS

(SEQ ID NO:144) and a light chain variable (VL) sequence of
 DVVMTQSPDSLAVSLGERATINCKSSQSLLSHNGNTYLHWYQQKPGQPPKLLINKVSTRFSGV
 PDRFSGSGSGTDFTLTISLQAEDVAVYYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:149) for
 binding to any one of the LAMP1 glycopeptides.

120. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of
 embodiments 1 to 10, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment
 competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH)
 sequence of

QVQLVQSGSELKKPGASVKVSCASGYTFTSAWMNWRQAPGQGLEWMGEIRTNAFNHAP
 YYAQGVKGRFVISRDDSVSTAYLQISSLKAEDTAVYYCAPNWDEGFAYWGQGLTVTVSS
 (SEQ ID NO:144) and a light chain variable (VL) sequence of
 DVVMTQSPDSLAVSLGERATINCKSSQSLLSHNGNTYLHWYQQKPGQPPKLLINKASTRESGV
 PDRFSGSGSGTDFTLTISLQAEDVAVYYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:150) for
 binding to any one of the LAMP1 glycopeptides.

121. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of
 embodiments 1 to 10, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment
 competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH)
 sequence of

QVQLVQSGSELKKPGASVKVSCASGYTFTSAWMNWRQAPGQGLEWMGEIRTNAFNHAP
 YYAQGVKGRFVISRDDSVSTAYLQISSLKAEDTAVYYCAPNWDEGFAYWGQGLTVTVSS
 (SEQ ID NO:144) and a light chain variable (VL) sequence of
 DVVMTQSPASLAVSPGQRATITCRSSQSLVSHNGNTYLHWYQQKPGQPPKLLINKVSNRFSG
 VPARFSGSGSGTDFTLTINPVEANDTANYFCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:151)
 for binding to any one of the LAMP1 glycopeptides.

122. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of
 embodiments 1 to 10, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment
 competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH)
 sequence of

QVQLVQSGSELKKPGASVKVSCASGYTFTSAWMNWRQAPGQGLEWMGEIRTNAFNHAP
 YYAQGVKGRFVISRDDSVSTAYLQISSLKAEDTAVYYCAPNWDEGFAYWGQGLTVTVSS
 (SEQ ID NO:144) and a light chain variable (VL) sequence of
 DVVLTQSPASLAVSPGQRATITCRSSESLSHSNGNTYLHWYQQKPGQPPKLLINKVSNKFTGV
 PARFSGSGSGTDFTLTINPVEANDTANYFCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:152) for
 binding to any one of the LAMP1 glycopeptides.

123. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of
 embodiments 1 to 10, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment
 competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH)
 sequence of

QVQLVQSGSELKKPGASVKVSCKASGYTFTSAWMNWRQAPGQGLEWMGEIRTNAFNHAP
 YYAQGVKGRFVISRDDSVSTAYLQISSLKAEDTAVYYCAPNWDEGFAYWGQGTLLTVSS
 (SEQ ID NO:144) and a light chain variable (VL) sequence of
 DVVLTQSPASLAVSPGQRATITCRASELSHSNANVYIHWWYQQKPGQPPKLLINKASNKFTGV
 PARFSGSGSGTDFTLTINPVEANDTANYCYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:153) for
 binding to any one of the LAMP1 glycopeptides.

124. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of
 embodiments 1 to 123, which specifically binds to COSMC knock-out T47D cells.

125. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124,
 wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody
 or antigen binding fragment comprising a heavy chain variable (VH) sequence of
 EVKLEESGGGLVQPGGSMKVSCGASGFTFSDAWMDWVRQSPEKGLEWVAEMRSKAFNHAI
 YYAESVKGRFTISRDDSKSRVYLQMNLLRPEDTGIYYCTPNWDEGFAYWGQGTLLTVSA
 (SEQ ID NO:1) and a light chain variable (VL) sequence of
 DVMLTQTPLSLPVSLGDQASISCRSSQSLVHSNGNTYLHWYLQKPGQSPKLLINKVSNRFFGV
 PDRFSGSGSGTDFTLKISRVEAEDLGVYFCSQSTHVPRTFGGGTKLEIK (SEQ ID NO:2) for
 binding to COSMC knock-out T47D cells.

126. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124,
 wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody
 or antigen binding fragment comprising a heavy chain variable (VH) sequence of
 EVKLEDSGGGLVQPGGSMKLSCAASGFTFSDAWMDWVRHSPEKGLEWVAELRSKAFNHAT
 YYAESVKGRFTISRDDSKSTVYLQMNSLRAEDTGIYYCTPNWDEGFAYWGQGTLLTVSA
 (SEQ ID NO:23) and a light chain variable (VL) sequence of
 NIMMTQSPSSLVVSAGEKVTMSCKSSHSVLYSSNQKNYLAWYQQKPGQSPKLLIYWASTKNS
 GVPDRFTGSGSGTDFTLTISVQAEDLAVYYCHQYLSSYTFGGGKLEIK (SEQ ID NO:24) for
 binding to COSMC knock-out T47D cells.

127. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124,
 wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody
 or antigen binding fragment comprising a heavy chain variable (VH) sequence of
 EVRLEESGGGLVQPGGSMKLSCVASGFTFSDAWMDWVRQSPERGLEWVAELRSKTFNHAT
 YYAESVRGRFTISRDDSKSTVYLQMNSLRAEDTGIYYCSPNWDEGFAYWGQGTLLTVSA
 (SEQ ID NO:45) and a light chain variable (VL) sequence of
 DVVMTQIPLSLCVSLGDQASISCRSSQSLVHNNGNTYLHWYLQKPGQSPKLLINKVSKRFTGV
 PDRFSGSGSGTDFTLKISRVEAEDLGVYFCSQSTHVPRTFGGGTKLEIK (SEQ ID NO:46) for
 binding to COSMC knock-out T47D cells.

128. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124,
 wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody
 or antigen binding fragment comprising a heavy chain variable (VH) sequence of

EVQLLESGGGLVQPGGSLRLSCAASGFTFSDAWMDWVRHAPGKGLEWVAELRSKAFNHATY
 YAESVKGRFTISRDDSKNTVYLQMNSLRAEDTAVYYCTPNWDEGFAYWGQGTLVTVSS (SEQ
 ID NO:133) and a light chain variable (VL) sequence of
 DVVMTQSPLSLPVTLGQPASISCRSSQSLVHSNGNTYLHWYQQRPGQSPRLLINKVSNRFSG
 VPDRFSGSGSGTDFTLKISRVEAEDVGVYFCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:145)
 for binding to COSMC knock-out T47D cells.

129. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of
 EVQLLESGGGLVQPGGSLRLSCAASGFTFSDAWMDWVRHAPGKGLEWVAELRSKAFNHATY
 YAESVKGRFTISRDDSKNTVYLQMNSLRAEDTAVYYCTPNWDEGFAYWGQGTLVTVSS (SEQ
 ID NO:133) and a light chain variable (VL) sequence of
 DVVMTQSPLSLPVTLGQPASISCRSSQSLVHSNGNTYLHWFQQRPGQSPRLLINKVSNRFSG
 VPDRFSGSGSGTDFTLKISRVEAEDVGVYFCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:146)
 for binding to COSMC knock-out T47D cells.

130. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of
 EVQLLESGGGLVQPGGSLRLSCAASGFTFSDAWMDWVRHAPGKGLEWVAELRSKAFNHATY
 YAESVKGRFTISRDDSKNTVYLQMNSLRAEDTAVYYCTPNWDEGFAYWGQGTLVTVSS (SEQ
 ID NO:133) and a light chain variable (VL) sequence of
 DVVMTQSPLSLPVTLGQPASISCRSSQSLVHSNANVYLHWFQQRPGQSPRLLINKVSNRFSGV
 PDRFSGSGSGTDFTLKISRVEAEDVGVYFCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:147) for
 binding to COSMC knock-out T47D cells.

131. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of
 EVQLLESGGGLVQPGGSLRLSCAASGFTFSDAWMDWVRHAPGKGLEWVAELRSKAFNHATY
 YAESVKGRFTISRDDSKNTVYLQMNSLRAEDTAVYYCTPNWDEGFAYWGQGTLVTVSS (SEQ
 ID NO:133) and a light chain variable (VL) sequence of
 DVVMTQSPDSLAVSLGERATINCRSSQSLVHSNGNTYLHWYQKPGQPPKLLINKVSNRFSG
 VPDRFSGSGSGTDFTLTISLQAEDVAVYFCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:148)
 for binding to COSMC knock-out T47D cells.

132. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of
 EVQLLESGGGLVQPGGSLRLSCAASGFTFSDAWMDWVRHAPGKGLEWVAELRSKAFNHATY
 YAESVKGRFTISRDDSKNTVYLQMNSLRAEDTAVYYCTPNWDEGFAYWGQGTLVTVSS (SEQ

ID NO:133) and a light chain variable (VL) sequence of DVVMTQSPDSLAVSLGERATINCKSSQSLLSNGNTYLHWYQQKPGQPPKLLINKVSTRFSGV PDRFSGSGSGTDFTLTISLQAEDVAVYYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:149) for binding to COSMC knock-out T47D cells.

133. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of EVQLLES GGGLVQPGGSLRLSCAASGFTFSDAWMDWVRHAPGKGLEWVAELRSKAFNHATY YAESVKGRFTISRDDSKNTVYLQMNSLRAEDTAVYYCTPNWDEGFAYWGQGLTVTVSS (SEQ ID NO:133) and a light chain variable (VL) sequence of DVVMTQSPDSLAVSLGERATINCKSSQSLLSNANVYLHWYQQKPGQPPKLLINKASTRESGV PDRFSGSGSGTDFTLTISLQAEDVAVYYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:150) for binding to COSMC knock-out T47D cells.

134. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of EVQLLES GGGLVQPGGSLRLSCAASGFTFSDAWMDWVRHAPGKGLEWVAELRSKAFNHATY YAESVKGRFTISRDDSKNTVYLQMNSLRAEDTAVYYCTPNWDEGFAYWGQGLTVTVSS (SEQ ID NO:133) and a light chain variable (VL) sequence of DVVMTQSPASLAVSPGQRATITCRSSQSLVHSNGNTYLHWYQQKPGQPPKLLINKVSNRFSV VPARFSGSGSGTDFTLTINPVEANDTANYFCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:151) for binding to COSMC knock-out T47D cells.

135. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of EVQLLES GGGLVQPGGSLRLSCAASGFTFSDAWMDWVRHAPGKGLEWVAELRSKAFNHATY YAESVKGRFTISRDDSKNTVYLQMNSLRAEDTAVYYCTPNWDEGFAYWGQGLTVTVSS (SEQ ID NO:133) and a light chain variable (VL) sequence of DVVLTQSPASLAVSPGQRATITCRSSESLSHSNGNTYLHWYQQKPGQPPKLLINKVSNKFTGV PARFSGSGSGTDFTLTINPVEANDTANYFCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:152) for binding to COSMC knock-out T47D cells.

136. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of EVQLLES GGGLVQPGGSLRLSCAASGFTFSDAWMDWVRHAPGKGLEWVAELRSKAFNHATY YAESVKGRFTISRDDSKNTVYLQMNSLRAEDTAVYYCTPNWDEGFAYWGQGLTVTVSS (SEQ ID NO:133) and a light chain variable (VL) sequence of DVVLTQSPASLAVSPGQRATITCRASESLSHSNANVYIHWYQQKPGQPPKLLINKASNKFTGV

PARFSGSGSGTDFTLTINPVEANDTANYCYCSQSTHVPRTFGGGKVEIK (SEQ ID NO:153) for binding to COSMC knock-out T47D cells.

137. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of EVQLLES GGGLVQPGGSLRLSCAASGFTFSDAWMDWVRQAPGKGLEWVSELRSKAFNHATY YAESVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCTPNWDEGFAYWGQGTLVTVSS (SEQ ID NO:134) and a light chain variable (VL) sequence of DVVMTQSPLSLPVTLGQPASISCRSSQSLVHSNGNTYLHWYQQRPGQSPRLLINKVSNRFSG VPDRFSGSGSGTDFTLKISRVEAEDVGVYFCSQSTHVPRTFGGGKVEIK (SEQ ID NO:145) for binding to COSMC knock-out T47D cells.

138. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of EVQLLES GGGLVQPGGSLRLSCAASGFTFSDAWMDWVRQAPGKGLEWVSELRSKAFNHATY YAESVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCTPNWDEGFAYWGQGTLVTVSS (SEQ ID NO:134) and a light chain variable (VL) sequence of DVVMTQSPLSLPVTLGQPASISCRSSQSLVHSNGNTYLHWFQQRPGQSPRLLINKVSNRFSG VPDRFSGSGSGTDFTLKISRVEAEDVGVYYCSQSTHVPRTFGGGKVEIK (SEQ ID NO:146) for binding to COSMC knock-out T47D cells.

139. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of EVQLLES GGGLVQPGGSLRLSCAASGFTFSDAWMDWVRQAPGKGLEWVSELRSKAFNHATY YAESVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCTPNWDEGFAYWGQGTLVTVSS (SEQ ID NO:134) and a light chain variable (VL) sequence of DVVMTQSPLSLPVTLGQPASISCRSSQSLVHSNANVYLHWFQQRPGQSPRLLINKVSNRFSGV PDRFSGSGSGTDFTLKISRVEAEDVGVYYCSQSTHVPRTFGGGKVEIK (SEQ ID NO:147) for binding to COSMC knock-out T47D cells.

140. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of EVQLLES GGGLVQPGGSLRLSCAASGFTFSDAWMDWVRQAPGKGLEWVSELRSKAFNHATY YAESVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCTPNWDEGFAYWGQGTLVTVSS (SEQ ID NO:134) and a light chain variable (VL) sequence of DVVMTQSPDSLAVSLGERATINCRSSQSLVHSNGNTYLHWYQQKPGQPPKLLINKVSNRFSG VPDRFSGSGSGTDFTLTISLQAEDVAVYFCSQSTHVPRTFGGGKVEIK (SEQ ID NO:148) for binding to COSMC knock-out T47D cells.

141. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of EVQLLES GGGGLVQP GGSRLS CAASGFTFSDAWMDWVRQAPGKGLEWVSELRSKAFNHATY YAESVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCTPNWDEGFAYWGQGTLVTVSS (SEQ ID NO:134) and a light chain variable (VL) sequence of DVVMTQSPDSLAVSLGERATINCKSSQSLLSHNGNTYLHWYQQKPGQPPKLLINKVSTRFSGV PDRFSGSGSGTDFTLTISLQAEDVAVYYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:149) for binding to COSMC knock-out T47D cells.

142. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of EVQLLES GGGGLVQP GGSRLS CAASGFTFSDAWMDWVRQAPGKGLEWVSELRSKAFNHATY YAESVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCTPNWDEGFAYWGQGTLVTVSS (SEQ ID NO:134) and a light chain variable (VL) sequence of DVVMTQSPDSLAVSLGERATINCKSSQSLLSHNGNTYLHWYQQKPGQPPKLLINKASTRESGV PDRFSGSGSGTDFTLTISLQAEDVAVYYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:150) for binding to COSMC knock-out T47D cells.

143. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of EVQLLES GGGGLVQP GGSRLS CAASGFTFSDAWMDWVRQAPGKGLEWVSELRSKAFNHATY YAESVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCTPNWDEGFAYWGQGTLVTVSS (SEQ ID NO:134) and a light chain variable (VL) sequence of DVVMTQSPASLAVSPGQRATITCRSSQSLVSHNGNTYLHWYQQKPGQPPKLLINKVSNRFSG VPARFSGSGSGTDFTLTINPVEANDTANYFCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:151) for binding to COSMC knock-out T47D cells.

144. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of EVQLLES GGGGLVQP GGSRLS CAASGFTFSDAWMDWVRQAPGKGLEWVSELRSKAFNHATY YAESVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCTPNWDEGFAYWGQGTLVTVSS (SEQ ID NO:134) and a light chain variable (VL) sequence of DVVLTQSPASLAVSPGQRATITCRSSQSLSHSNGNTYLHWYQQKPGQPPKLLINKVSNKFTGV PARFSGSGSGTDFTLTINPVEANDTANYFCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:152) for binding to COSMC knock-out T47D cells.

145. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody

or antigen binding fragment comprising a heavy chain variable (VH) sequence of EVQLLES GGGGLVQPGGSLRLS CAASGFTFSDAWMDWVRQAPGKGLEWVSELRSKAFNHATY YAESVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCTPNWDEGFAYWGQGTLVTVSS (SEQ ID NO:134) and a light chain variable (VL) sequence of DVVLTQSPASLAVSPGQRATITCRASELSHSNANVYIHWYQQKPGQPPKLLINKASNKFTGV PARFSGSGSGTDFTLTINPVEANDTANYCYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:153) for binding to COSMC knock-out T47D cells.

146. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of EVQLLES GGGGLVQPGGSLRLS CAASGFTFSDAWMDWVRQAPGKGLEWVSEIRSSAFNHATY YAESVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCTPNWDEGFAYWGQGTLVTVSS (SEQ ID NO:135) and a light chain variable (VL) sequence of DVVMTQSPLSLPVTLGQPASISCRSSQSLVHSNGNTYLHWYQQRPQGQSPRLLINKVSNRFSG VPDRFSGSGSGTDFTLKISRVEAEDVGVYFCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:145) for binding to COSMC knock-out T47D cells.

147. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of EVQLLES GGGGLVQPGGSLRLS CAASGFTFSDAWMDWVRQAPGKGLEWVSEIRSSAFNHATY YAESVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCTPNWDEGFAYWGQGTLVTVSS (SEQ ID NO:135) and a light chain variable (VL) sequence of DVVMTQSPLSLPVTLGQPASISCRSSQSLVHSNGNTYLHWFQQRPQGQSPRLLINKVSNRFSG VPDRFSGSGSGTDFTLKISRVEAEDVGVYYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:146) for binding to COSMC knock-out T47D cells.

148. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of EVQLLES GGGGLVQPGGSLRLS CAASGFTFSDAWMDWVRQAPGKGLEWVSEIRSSAFNHATY YAESVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCTPNWDEGFAYWGQGTLVTVSS (SEQ ID NO:135) and a light chain variable (VL) sequence of DVVMTQSPLSLPVTLGQPASISCRSSQSLVHSNANVYLHWFQQRPQGQSPRLLINKVSNRFSGV PDRFSGSGSGTDFTLKISRVEAEDVGVYYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:147) for binding to COSMC knock-out T47D cells.

149. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of EVQLLES GGGGLVQPGGSLRLS CAASGFTFSDAWMDWVRQAPGKGLEWVSEIRSSAFNHATY

YAESVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCTPNWDEGFAYWGQGLTVTVSS (SEQ ID NO:135) and a light chain variable (VL) sequence of DVVMTQSPDSLAVSLGERATINCRSSQSLVHSNGNTYLHWYQQKPGQPPKLLINKVSNRFSGVPDRFSGSGSGTDFTLTISLQAEDVAVYFCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:148) for binding to COSMC knock-out T47D cells.

150. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of EVQLLES GGGLVQPGGSLRLS CAASGFTFSDAWMDWVRQAPGKGLEWVSEIRSSAFNHATY YAESVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCTPNWDEGFAYWGQGLTVTVSS (SEQ ID NO:135) and a light chain variable (VL) sequence of DVVMTQSPDSLAVSLGERATINCKSSQSLLSHNGNTYLHWYQQKPGQPPKLLINKVSTRFSGVPDRFSGSGSGTDFTLTISLQAEDVAVYYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:149) for binding to COSMC knock-out T47D cells.

151. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of EVQLLES GGGLVQPGGSLRLS CAASGFTFSDAWMDWVRQAPGKGLEWVSEIRSSAFNHATY YAESVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCTPNWDEGFAYWGQGLTVTVSS (SEQ ID NO:135) and a light chain variable (VL) sequence of DVVMTQSPDSLAVSLGERATINCKSSQSLLSHNSANVYLHWYQQKPGQPPKLLINKASTRESGV PDRFSGSGSGTDFTLTISLQAEDVAVYYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:150) for binding to COSMC knock-out T47D cells.

152. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of EVQLLES GGGLVQPGGSLRLS CAASGFTFSDAWMDWVRQAPGKGLEWVSEIRSSAFNHATY YAESVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCTPNWDEGFAYWGQGLTVTVSS (SEQ ID NO:135) and a light chain variable (VL) sequence of DVVMTQSPASLAVSPGQRATITCRSSQSLVHSNGNTYLHWYQQKPGQPPKLLINKVSNRFSGV PARFSGSGSGTDFTLTINPVEANDTANYFCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:151) for binding to COSMC knock-out T47D cells.

153. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of EVQLLES GGGLVQPGGSLRLS CAASGFTFSDAWMDWVRQAPGKGLEWVSEIRSSAFNHATY YAESVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCTPNWDEGFAYWGQGLTVTVSS (SEQ ID NO:135) and a light chain variable (VL) sequence of

DVVLTSQSPASLAVSPGQRATITCRSSESLSHSNGNTYLHWYQQKPGQPPKLLINKVSNKFTGV
PARFSGSGSGTDFTLTINPVEANDTANYCYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:152) for
binding to COSMC knock-out T47D cells.

154. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124,
wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody
or antigen binding fragment comprising a heavy chain variable (VH) sequence of
EVQLLESQGGGLVQPGGSLRLSQAASGFTFSDAWMDWVRQAPGKGLEWVSEIRSSAFNHATY
YAESVKGRFTISRDDSKNTLYLQMNSLRADTAIVYYCTPNWDEGFAYWGQGTLLTVSS (SEQ
ID NO:135) and a light chain variable (VL) sequence of
DVVLTSQSPASLAVSPGQRATITCRASESLSHSNANVYIHWYQQKPGQPPKLLINKASNKFTGV
PARFSGSGSGTDFTLTINPVEANDTANYCYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:153) for
binding to COSMC knock-out T47D cells.

155. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124,
wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody
or antigen binding fragment comprising a heavy chain variable (VH) sequence of
EVQLVESGGGLVQPGGSLRLSQAASGFTFSDAWMDWVRHAPGKGLEWVAELRSKAFNHATY
YAESVKGRFTISRDDSKNTVYLQMNSLKTEDTAIVYYCTPNWDEGFAYWGQGTLLTVSS (SEQ
ID NO:136) and a light chain variable (VL) sequence of
DVVMTQSPLSLPVTLGQPASISCRSSQSLVHSNGNTYLHWYQQRPQGQSPRLLINKVSNRFSG
VPDRFSGSGSGTDFTLKISRVEAEDVGVYFCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:145)
for binding to COSMC knock-out T47D cells.

156. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124,
wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody
or antigen binding fragment comprising a heavy chain variable (VH) sequence of
EVQLVESGGGLVQPGGSLRLSQAASGFTFSDAWMDWVRHAPGKGLEWVAELRSKAFNHATY
YAESVKGRFTISRDDSKNTVYLQMNSLKTEDTAIVYYCTPNWDEGFAYWGQGTLLTVSS (SEQ
ID NO:136) and a light chain variable (VL) sequence of
DVVMTQSPLSLPVTLGQPASISCRSSQSLVHSNGNTYLHWFQQRPQGQSPRLLINKVSNRFSG
VPDRFSGSGSGTDFTLKISRVEAEDVGVYCYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:146)
for binding to COSMC knock-out T47D cells.

157. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124,
wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody
or antigen binding fragment comprising a heavy chain variable (VH) sequence of
EVQLVESGGGLVQPGGSLRLSQAASGFTFSDAWMDWVRHAPGKGLEWVAELRSKAFNHATY
YAESVKGRFTISRDDSKNTVYLQMNSLKTEDTAIVYYCTPNWDEGFAYWGQGTLLTVSS (SEQ
ID NO:136) and a light chain variable (VL) sequence of
DVVMTQSPLSLPVTLGQPASISCRSSQSLVHSNANVYLHWFQQRPQGQSPRLLINKVSNRFSGV

PDRFSGSGSGTDFTLKISRVEAEDVGVYYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:147) for binding to COSMC knock-out T47D cells.

158. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of EVQLVESGGGLVKPGGSLRLSCAASGFTFSDAWMDWVRHAPGKGLEWVAELRSKAFNHATY YAESVKGRFTISRDDSKNTVYLQMNSLKTEDTAVYYCTPNWDEGFAYWGQGLTVTVSS (SEQ ID NO:136) and a light chain variable (VL) sequence of DVVMTQSPDSLAVSLGERATINCRSSQSLVHSNGNTYLHWYQQKPGQPPKLLINKVSNRFSG VPDRFSGSGSGTDFTLTISLQAEDVAVYFCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:148) for binding to COSMC knock-out T47D cells.

159. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of EVQLVESGGGLVKPGGSLRLSCAASGFTFSDAWMDWVRHAPGKGLEWVAELRSKAFNHATY YAESVKGRFTISRDDSKNTVYLQMNSLKTEDTAVYYCTPNWDEGFAYWGQGLTVTVSS (SEQ ID NO:136) and a light chain variable (VL) sequence of DVVMTQSPDSLAVSLGERATINCKSSQSLLSNGNTYLHWYQQKPGQPPKLLINKVSTRFSGV PDRFSGSGSGTDFTLTISLQAEDVAVYYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:149) for binding to COSMC knock-out T47D cells.

160. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of EVQLVESGGGLVKPGGSLRLSCAASGFTFSDAWMDWVRHAPGKGLEWVAELRSKAFNHATY YAESVKGRFTISRDDSKNTVYLQMNSLKTEDTAVYYCTPNWDEGFAYWGQGLTVTVSS (SEQ ID NO:136) and a light chain variable (VL) sequence of DVVMTQSPDSLAVSLGERATINCKSSQSLLSNANVYLHWYQQKPGQPPKLLINKASTRESGV PDRFSGSGSGTDFTLTISLQAEDVAVYYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:150) for binding to COSMC knock-out T47D cells.

161. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of EVQLVESGGGLVKPGGSLRLSCAASGFTFSDAWMDWVRHAPGKGLEWVAELRSKAFNHATY YAESVKGRFTISRDDSKNTVYLQMNSLKTEDTAVYYCTPNWDEGFAYWGQGLTVTVSS (SEQ ID NO:136) and a light chain variable (VL) sequence of DVVMTQSPASLAVSPGQRATITCRSSQSLVHSNGNTYLHWYQQKPGQPPKLLINKVSNRFSG VPARFSGSGSGTDFTLTINPVEANDTANYFCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:151) for binding to COSMC knock-out T47D cells.

162. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of EVQLVESGGGLVKPGGSLRLSCAASGFTFSDAWMDWVRHAPGKGLEWVAELRSKAFNHATY YAESVKGRFTISRDDSKNTVYLQMNSLKTEDTAVYYCTPNWDEGFAYWGQGTLVTVSS (SEQ ID NO:136) and a light chain variable (VL) sequence of DVVLTQSPASLAVSPGQRATITCRSSESLSHSNGNTYLHWYQQKPGQPPKLLINKVSNKFTGV PARFSGSGSGTDFTLTINPVEANDTANYYYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:152) for binding to COSMC knock-out T47D cells.

163. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of EVQLVESGGGLVKPGGSLRLSCAASGFTFSDAWMDWVRHAPGKGLEWVAELRSKAFNHATY YAESVKGRFTISRDDSKNTVYLQMNSLKTEDTAVYYCTPNWDEGFAYWGQGTLVTVSS (SEQ ID NO:136) and a light chain variable (VL) sequence of DVVLTQSPASLAVSPGQRATITCRASESLSHSNANVYIHWYQQKPGQPPKLLINKASNKFTGV PARFSGSGSGTDFTLTINPVEANDTANYYYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:153) for binding to COSMC knock-out T47D cells.

164. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of EVQLVESGGGLVKPGGSLRLSCAASGFTFSDAWMDWVRQAPGKGLEWVGELRSKAFNHAT YYAESVKGRFTISRDDSKNTLYLQMNSLKTEDTAVYYCTPNWDEGFAYWGQGTLVTVSS (SEQ ID NO:137) and a light chain variable (VL) sequence of DVVMTQSPLSLPVTLGQPASISCRSSQSLVHSNGNTYLHWYQQRPQGQSPRLLINKVSNRFSG VPDRFSGSGSGTDFTLKISRVEAEDVGVYFCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:145) for binding to COSMC knock-out T47D cells.

165. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of EVQLVESGGGLVKPGGSLRLSCAASGFTFSDAWMDWVRQAPGKGLEWVGELRSKAFNHAT YYAESVKGRFTISRDDSKNTLYLQMNSLKTEDTAVYYCTPNWDEGFAYWGQGTLVTVSS (SEQ ID NO:137) and a light chain variable (VL) sequence of DVVMTQSPLSLPVTLGQPASISCRSSQSLVHSNGNTYLHWFQQRPQGQSPRLLINKVSNRFSG VPDRFSGSGSGTDFTLKISRVEAEDVGVYYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:146) for binding to COSMC knock-out T47D cells.

166. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody

or antigen binding fragment comprising a heavy chain variable (VH) sequence of
 EVQLVESGGGLVKPGGSLRLSCAASGFTFSDAWMDWVRQAPGKGLEWVGELRSKAFNHAT
 YYAESVKGRFTISRDDSKNTLYLQMNSLKTEDTAVYYCTPNWDEGFAYWGQGTLVTVSS
 (SEQ ID NO:137) and a light chain variable (VL) sequence of
 DVVMTQSPSLPVTLGQPASISCRSSQSLVHSNANVYLHWYFQQRPQGSPRLLINKVSNRFSGV
 PDRFSGSGSGTDFTLKISRVEAEDVGVYYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:147) for
 binding to COSMC knock-out T47D cells.

167. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124,
 wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody
 or antigen binding fragment comprising a heavy chain variable (VH) sequence of
 EVQLVESGGGLVKPGGSLRLSCAASGFTFSDAWMDWVRQAPGKGLEWVGELRSKAFNHAT
 YYAESVKGRFTISRDDSKNTLYLQMNSLKTEDTAVYYCTPNWDEGFAYWGQGTLVTVSS
 (SEQ ID NO:137) and a light chain variable (VL) sequence of
 DVVMTQSPDSLAVSLGERATINCRSSQSLVHSNGNTYLHWYQQKPGQPPKLLINKVSNRFSG
 VPDRFSGSGSGTDFTLTISLQAEDVAVYFCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:148)
 for binding to COSMC knock-out T47D cells.

168. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124,
 wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody
 or antigen binding fragment comprising a heavy chain variable (VH) sequence of
 EVQLVESGGGLVKPGGSLRLSCAASGFTFSDAWMDWVRQAPGKGLEWVGELRSKAFNHAT
 YYAESVKGRFTISRDDSKNTLYLQMNSLKTEDTAVYYCTPNWDEGFAYWGQGTLVTVSS
 (SEQ ID NO:137) and a light chain variable (VL) sequence of
 DVVMTQSPDSLAVSLGERATINCKSSQSLHNSNGNTYLHWYQQKPGQPPKLLINKVSTRFSGV
 PDRFSGSGSGTDFTLTISLQAEDVAVYYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:149) for
 binding to COSMC knock-out T47D cells.

169. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124,
 wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody
 or antigen binding fragment comprising a heavy chain variable (VH) sequence of
 EVQLVESGGGLVKPGGSLRLSCAASGFTFSDAWMDWVRQAPGKGLEWVGELRSKAFNHAT
 YYAESVKGRFTISRDDSKNTLYLQMNSLKTEDTAVYYCTPNWDEGFAYWGQGTLVTVSS
 (SEQ ID NO:137) and a light chain variable (VL) sequence of
 DVVMTQSPDSLAVSLGERATINCKSSQSLHNSNANVYLHWYQQKPGQPPKLLINKASTRESGV
 PDRFSGSGSGTDFTLTISLQAEDVAVYYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:150) for
 binding to COSMC knock-out T47D cells.

170. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124,
 wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody
 or antigen binding fragment comprising a heavy chain variable (VH) sequence of
 EVQLVESGGGLVKPGGSLRLSCAASGFTFSDAWMDWVRQAPGKGLEWVGELRSKAFNHAT

YYAESVKGRFTISRDDSKNTLYLQMNSLKTEDTAVYYCTPNWDEGFAYWGQGLTVTVSS (SEQ ID NO:137) and a light chain variable (VL) sequence of DVVMTQSPASLAVSPGQRATITCRSSQSLVHSNGNTYLHWYQQKPGQPPKLLINKVSNRFSG VPARFSGSGSGTDFTLTINPVEANDTANYFCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:151) for binding to COSMC knock-out T47D cells.

171. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of EVQLVESGGGLVKPGGSLRLSCAASGFTFSDAWMDWVRQAPGKGLEWVGELRSKAFNHAT YYAESVKGRFTISRDDSKNTLYLQMNSLKTEDTAVYYCTPNWDEGFAYWGQGLTVTVSS (SEQ ID NO:137) and a light chain variable (VL) sequence of DVVLTQSPASLAVSPGQRATITCRSSQSLVHSNGNTYLHWYQQKPGQPPKLLINKVSNKFTGV PARFSGSGSGTDFTLTINPVEANDTANYFCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:152) for binding to COSMC knock-out T47D cells.

172. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of EVQLVESGGGLVKPGGSLRLSCAASGFTFSDAWMDWVRQAPGKGLEWVGELRSKAFNHAT YYAESVKGRFTISRDDSKNTLYLQMNSLKTEDTAVYYCTPNWDEGFAYWGQGLTVTVSS (SEQ ID NO:137) and a light chain variable (VL) sequence of DVVLTQSPASLAVSPGQRATITCRASESLSHSNANVYIHWYQQKPGQPPKLLINKASNKFTGV PARFSGSGSGTDFTLTINPVEANDTANYFCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:153) for binding to COSMC knock-out T47D cells.

173. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of EVQLVESGGGLVKPGGSLRLSCAASGFTFSDAWMDWVRQAPGKGLEWVGELRSKAFNHATY YAEPVKGRFTISRDDSKNTLYLQMNSLKTEDTAVYYCTPNWDEGFAYWGQGLTVTVSS (SEQ ID NO:138) and a light chain variable (VL) sequence of DVVMTQSPSLPVTLGQPASISCRSSQSLVHSNGNTYLHWYQQRPQGQSPRLLINKVSNRFSG VPDRFSGSGSGTDFTLTISRVEAEDVGVYFCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:145) for binding to COSMC knock-out T47D cells.

174. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of EVQLVESGGGLVKPGGSLRLSCAASGFTFSDAWMDWVRQAPGKGLEWVGELRSKAFNHATY YAEPVKGRFTISRDDSKNTLYLQMNSLKTEDTAVYYCTPNWDEGFAYWGQGLTVTVSS (SEQ ID NO:138) and a light chain variable (VL) sequence of

DVVMTQSPLSLPVTLGQPASISCRSSQSLVHSNGNTYLHWFQQRPGQSPRLLINKVSNRFSG
VPDRFSGSGSGTDFTLKISRVEAEDVGVYYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:146)
for binding to COSMC knock-out T47D cells.

175. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of EVQLVESGGGLVKPGGSLRLSCAASGFTFSDAWMDWVRQAPGKGLEWGEIRSKAFNHATY YAEPVKGRFTISRDDSKNTLYLQMNSLKTEDTAVYYCTPNWDEGFAYWGQGTLLTVSS (SEQ ID NO:138) and a light chain variable (VL) sequence of DVVMTQSPLSLPVTLGQPASISCRSSQSLVHSNANVYLHWFQQRPGQSPRLLINKVSNRFSGV PDRFSGSGSGTDFTLKISRVEAEDVGVYYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:147) for binding to COSMC knock-out T47D cells.

176. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of EVQLVESGGGLVKPGGSLRLSCAASGFTFSDAWMDWVRQAPGKGLEWGEIRSKAFNHATY YAEPVKGRFTISRDDSKNTLYLQMNSLKTEDTAVYYCTPNWDEGFAYWGQGTLLTVSS (SEQ ID NO:138) and a light chain variable (VL) sequence of DVVMTQSPDSLAVSLGERATINCRSSQSLVHSNGNTYLHWYQQKPGQPPKLLINKVSNRFSG VPDRFSGSGSGTDFTLTISLQAEDVAVYFCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:148) for binding to COSMC knock-out T47D cells.

177. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of EVQLVESGGGLVKPGGSLRLSCAASGFTFSDAWMDWVRQAPGKGLEWGEIRSKAFNHATY YAEPVKGRFTISRDDSKNTLYLQMNSLKTEDTAVYYCTPNWDEGFAYWGQGTLLTVSS (SEQ ID NO:138) and a light chain variable (VL) sequence of DVVMTQSPDSLAVSLGERATINCKSSQSLHNSNGNTYLHWYQQKPGQPPKLLINKVSTRFSGV PDRFSGSGSGTDFTLTISLQAEDVAVYYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:149) for binding to COSMC knock-out T47D cells.

178. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of EVQLVESGGGLVKPGGSLRLSCAASGFTFSDAWMDWVRQAPGKGLEWGEIRSKAFNHATY YAEPVKGRFTISRDDSKNTLYLQMNSLKTEDTAVYYCTPNWDEGFAYWGQGTLLTVSS (SEQ ID NO:138) and a light chain variable (VL) sequence of DVVMTQSPDSLAVSLGERATINCKSSQSLHNSNANVYLHWYQQKPGQPPKLLINKASTRESGV

PDRFSGSGSGTDFTLTISLQAEDVAVYYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:150) for binding to COSMC knock-out T47D cells.

179. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of EVQLVESGGGLVKPGGSLRLSCAASGFTFSDAWMDWVRQAPGKGLEWVGEIRSKAFNHATY YAEPVKGRFTISRDDSKNTLYLQMNSLKTEDTAVYYCTPNWDEGFAYWGQGTLLTVSS (SEQ ID NO:138) and a light chain variable (VL) sequence of DVVMTQSPASLAVSPGQRATITCRSSQSLVHSNGNTYLHWYQQKPGQPPKLLINKVSNRFSG VPARFSGSGSGTDFTLTINPVEANDTANYFCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:151) for binding to COSMC knock-out T47D cells.

180. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of EVQLVESGGGLVKPGGSLRLSCAASGFTFSDAWMDWVRQAPGKGLEWVGEIRSKAFNHATY YAEPVKGRFTISRDDSKNTLYLQMNSLKTEDTAVYYCTPNWDEGFAYWGQGTLLTVSS (SEQ ID NO:138) and a light chain variable (VL) sequence of DVVLTQSPASLAVSPGQRATITCRSSQSLVHSNGNTYLHWYQQKPGQPPKLLINKVSNKFTGV PARFSGSGSGTDFTLTINPVEANDTANYFCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:152) for binding to COSMC knock-out T47D cells.

181. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of EVQLVESGGGLVKPGGSLRLSCAASGFTFSDAWMDWVRQAPGKGLEWVGEIRSKAFNHATY YAEPVKGRFTISRDDSKNTLYLQMNSLKTEDTAVYYCTPNWDEGFAYWGQGTLLTVSS (SEQ ID NO:138) and a light chain variable (VL) sequence of DVVLTQSPASLAVSPGQRATITCRASELSHSNANVYIHWYQQKPGQPPKLLINKASNKFTGV PARFSGSGSGTDFTLTINPVEANDTANYFCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:153) for binding to COSMC knock-out T47D cells.

182. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of EVQLVESGGGLVQPGGSLRLSCAASGFTFSDAWMDWVRHAPGKGLEWVAELRSKAFNHATY YAESVKGRFTISRDDSKNSVYLYQMNSLKTEDTAVYYCTPNWDEGFAYWGQGTLLTVSS (SEQ ID NO:139) and a light chain variable (VL) sequence of DVVMTQSPLSLPVTLGQPASISCRSSQSLVHSNGNTYLHWYQQRPGQSPRLLINKVSNRFSG VPDRFSGSGSGTDFTLTKISRVEAEDVGVYFCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:145) for binding to COSMC knock-out T47D cells.

183. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of EVQLVESGGGLVQPGGSLRLSCAASGFTFSDAWMDWVRHAPGKGLEWVAELRSKAFNHATY YAESVKGRFTISRDDSKNSVYLQMNSLKTEDTAVYYCTPNWDEGFAYWGQGTLVTVSS (SEQ ID NO:139) and a light chain variable (VL) sequence of DVVMTQSPLSLPVTLGQPASISCRSSQSLVHSNGNTYLHWFQQRPGQSPRLLINKVSNRFGSG VPDRFSGSGSGTDFTLKISRVEAEDVGVYYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:146) for binding to COSMC knock-out T47D cells.

184. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of EVQLVESGGGLVQPGGSLRLSCAASGFTFSDAWMDWVRHAPGKGLEWVAELRSKAFNHATY YAESVKGRFTISRDDSKNSVYLQMNSLKTEDTAVYYCTPNWDEGFAYWGQGTLVTVSS (SEQ ID NO:139) and a light chain variable (VL) sequence of DVVMTQSPLSLPVTLGQPASISCRSSQSLVHSNANVYLHWFQQRPGQSPRLLINKVSNRFGSGV PDRFSGSGSGTDFTLKISRVEAEDVGVYYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:147) for binding to COSMC knock-out T47D cells.

185. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of EVQLVESGGGLVQPGGSLRLSCAASGFTFSDAWMDWVRHAPGKGLEWVAELRSKAFNHATY YAESVKGRFTISRDDSKNSVYLQMNSLKTEDTAVYYCTPNWDEGFAYWGQGTLVTVSS (SEQ ID NO:139) and a light chain variable (VL) sequence of DVVMTQSPDSLAVSLGERATINCRSSQSLVHSNGNTYLHWYQQKPGQPPKLLINKVSNRFGSG VPDRFSGSGSGTDFTLTISLQAEDVAVYFCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:148) for binding to COSMC knock-out T47D cells.

186. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of EVQLVESGGGLVQPGGSLRLSCAASGFTFSDAWMDWVRHAPGKGLEWVAELRSKAFNHATY YAESVKGRFTISRDDSKNSVYLQMNSLKTEDTAVYYCTPNWDEGFAYWGQGTLVTVSS (SEQ ID NO:139) and a light chain variable (VL) sequence of DVVMTQSPDSLAVSLGERATINCKSSQSLHSNGNTYLHWYQQKPGQPPKLLINKVSTRFGSGV PDRFSGSGSGTDFTLTISLQAEDVAVYYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:149) for binding to COSMC knock-out T47D cells.

187. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody

or antigen binding fragment comprising a heavy chain variable (VH) sequence of EVQLVESGGGLVQPGGSLRLSCAASGFTFSDAWMDWVRHAPGKGLEWVAELRSKAFNHATY YAESVKGRFTISRDDSKNSVYLQMNSLKTEDTAVYYCTPNWDEGFAYWGQGLTVTVSS (SEQ ID NO:139) and a light chain variable (VL) sequence of DVVMTQSPDSLAVSLGERATINCKSSQSLLSNANVYLHWYQQKPGQPPKLLINKASTRESGV PDRFSGSGSGTDFTLTISLQAEDVAVYYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:150) for binding to COSMC knock-out T47D cells.

188. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of EVQLVESGGGLVQPGGSLRLSCAASGFTFSDAWMDWVRHAPGKGLEWVAELRSKAFNHATY YAESVKGRFTISRDDSKNSVYLQMNSLKTEDTAVYYCTPNWDEGFAYWGQGLTVTVSS (SEQ ID NO:139) and a light chain variable (VL) sequence of DVVMTQSPASLAVSPGQRATITCRSSQSLVHSNGNTYLHWYQQKPGQPPKLLINKVSNRFSV VPARFSGSGSGTDFTLTINPVEANDTANYFCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:151) for binding to COSMC knock-out T47D cells.

189. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of EVQLVESGGGLVQPGGSLRLSCAASGFTFSDAWMDWVRHAPGKGLEWVAELRSKAFNHATY YAESVKGRFTISRDDSKNSVYLQMNSLKTEDTAVYYCTPNWDEGFAYWGQGLTVTVSS (SEQ ID NO:139) and a light chain variable (VL) sequence of DVVLTQSPASLAVSPGQRATITCRSSESLSHSNGNTYLHWYQQKPGQPPKLLINKVSNKFTGV PARFSGSGSGTDFTLTINPVEANDTANYFCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:152) for binding to COSMC knock-out T47D cells.

190. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of EVQLVESGGGLVQPGGSLRLSCAASGFTFSDAWMDWVRHAPGKGLEWVAELRSKAFNHATY YAESVKGRFTISRDDSKNSVYLQMNSLKTEDTAVYYCTPNWDEGFAYWGQGLTVTVSS (SEQ ID NO:139) and a light chain variable (VL) sequence of DVVLTQSPASLAVSPGQRATITCRASELSHSNANVYIHWYQQKPGQPPKLLINKASNKFTGV PARFSGSGSGTDFTLTINPVEANDTANYFCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:153) for binding to COSMC knock-out T47D cells.

191. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of EVQLVESGGGLVQPGGSLRLSCAASGFTFSDAWMDWVRQAPGKGLEWVGELRSKAFNHAT

YYAESVKGRFTISRDDSKNSLYLQMNSLKTEDTAVYYCTPNWDEGFAYWGQGTLVTVSS
(SEQ ID NO:140) and a light chain variable (VL) sequence of
DVVMTQSPLSLPVTLGQPASISCRSSQSLVHSNGNTYLHWYQQRPGQSPRLLINKVSNRFSG
VPDRFSGSGSGTDFTLKISRVEAEDVGVYFCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:145)
for binding to COSMC knock-out T47D cells.

192. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of
EVQLVESGGGLVQPGGSLRLSCAASGFTFSDAWMDWVRQAPGKGLEWVGELRSKAFNHAT
YYAESVKGRFTISRDDSKNSLYLQMNSLKTEDTAVYYCTPNWDEGFAYWGQGTLVTVSS
(SEQ ID NO:140) and a light chain variable (VL) sequence of
DVVMTQSPLSLPVTLGQPASISCRSSQSLVHSNGNTYLHWFQQRPGQSPRLLINKVSNRFSG
VPDRFSGSGSGTDFTLKISRVEAEDVGVYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:146)
for binding to COSMC knock-out T47D cells.

193. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of
EVQLVESGGGLVQPGGSLRLSCAASGFTFSDAWMDWVRQAPGKGLEWVGELRSKAFNHAT
YYAESVKGRFTISRDDSKNSLYLQMNSLKTEDTAVYYCTPNWDEGFAYWGQGTLVTVSS
(SEQ ID NO:140) and a light chain variable (VL) sequence of
DVVMTQSPLSLPVTLGQPASISCRSSQSLVHSNANVYLHWFQQRPGQSPRLLINKVSNRFSGV
PDRFSGSGSGTDFTLKISRVEAEDVGVYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:147) for
binding to COSMC knock-out T47D cells.

194. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of
EVQLVESGGGLVQPGGSLRLSCAASGFTFSDAWMDWVRQAPGKGLEWVGELRSKAFNHAT
YYAESVKGRFTISRDDSKNSLYLQMNSLKTEDTAVYYCTPNWDEGFAYWGQGTLVTVSS
(SEQ ID NO:140) and a light chain variable (VL) sequence of
DVVMTQSPDSLAVSLGERATINCRSSQSLVHSNGNTYLHWYQQKPGQPPKLLINKVSNRFSG
VPDRFSGSGSGTDFTLTISLQAEDVAVYFCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:148)
for binding to COSMC knock-out T47D cells.

195. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of
EVQLVESGGGLVQPGGSLRLSCAASGFTFSDAWMDWVRQAPGKGLEWVGELRSKAFNHAT
YYAESVKGRFTISRDDSKNSLYLQMNSLKTEDTAVYYCTPNWDEGFAYWGQGTLVTVSS
(SEQ ID NO:140) and a light chain variable (VL) sequence of

DVVMTQSPDSLAVSLGERATINCKSSQSLHNSNGNTYLHWYQQKPGQPPKLLINKVSTRFSGV
PDRFSGSGSGTDFTLTISLQAEDVAVYYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:149) for
binding to COSMC knock-out T47D cells.

196. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124,
wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody
or antigen binding fragment comprising a heavy chain variable (VH) sequence of
EVQLVESGGGLVQPGGSLRLSCAASGFTFSDAWMDWVRQAPGKGLEWVGELRSKAFNHAT
YYAESVKGRFTISRDDSKNSLYLQMNSLKTEDTAVYYCTPNWDEGFAYWGQGTLLTVSS
(SEQ ID NO:140) and a light chain variable (VL) sequence of
DVVMTQSPDSLAVSLGERATINCKSSQSLHNSNANVYLHWYQQKPGQPPKLLINKASTRESGV
PDRFSGSGSGTDFTLTISLQAEDVAVYYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:150) for
binding to COSMC knock-out T47D cells.

197. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124,
wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody
or antigen binding fragment comprising a heavy chain variable (VH) sequence of
EVQLVESGGGLVQPGGSLRLSCAASGFTFSDAWMDWVRQAPGKGLEWVGELRSKAFNHAT
YYAESVKGRFTISRDDSKNSLYLQMNSLKTEDTAVYYCTPNWDEGFAYWGQGTLLTVSS
(SEQ ID NO:140) and a light chain variable (VL) sequence of
DVVMTQSPASLAVSPGQRATITCRSSQSLVHNSNGNTYLHWYQQKPGQPPKLLINKVSNRFSG
VPAFSGSGSGTDFTLTINPVEANDTANYFCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:151)
for binding to COSMC knock-out T47D cells.

198. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124,
wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody
or antigen binding fragment comprising a heavy chain variable (VH) sequence of
EVQLVESGGGLVQPGGSLRLSCAASGFTFSDAWMDWVRQAPGKGLEWVGELRSKAFNHAT
YYAESVKGRFTISRDDSKNSLYLQMNSLKTEDTAVYYCTPNWDEGFAYWGQGTLLTVSS
(SEQ ID NO:140) and a light chain variable (VL) sequence of
DVVLTQSPASLAVSPGQRATITCRSSESLSHSNGNTYLHWYQQKPGQPPKLLINKVSNKFTGV
PARFSGSGSGTDFTLTINPVEANDTANYFCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:152) for
binding to COSMC knock-out T47D cells.

199. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124,
wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody
or antigen binding fragment comprising a heavy chain variable (VH) sequence of
EVQLVESGGGLVQPGGSLRLSCAASGFTFSDAWMDWVRQAPGKGLEWVGELRSKAFNHAT
YYAESVKGRFTISRDDSKNSLYLQMNSLKTEDTAVYYCTPNWDEGFAYWGQGTLLTVSS
(SEQ ID NO:140) and a light chain variable (VL) sequence of
DVVLTQSPASLAVSPGQRATITCRASESLSHSNANVYIHWYQQKPGQPPKLLINKASNKFTGV

PARFSGSGSGTDFTLTINPVEANDTANYYCSQSTHVPRTFGGGKVEIK (SEQ ID NO:153) for binding to COSMC knock-out T47D cells.

200. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of EVQLVESGGGLVQPGGSLRLSCAASGFTFSDAWMDWVRQAPGKGLEWVGETRSKAFNYAT YYAESVKGRFTISRDDSKNSLYLQMNSLKTEDTAVYYCTPNWDEGFAYWGQGTLVTVSS (SEQ ID NO:141) and a light chain variable (VL) sequence of DVVMTQSPLSLPVTLGQPASISCRSSQSLVHSNGNTYLHWYQQRPGQSPRLLINKVSNRFSG VPDRFSGSGSGTDFTLKISRVEAEDVGVYFCSQSTHVPRTFGGGKVEIK (SEQ ID NO:145) for binding to COSMC knock-out T47D cells.

201. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of EVQLVESGGGLVQPGGSLRLSCAASGFTFSDAWMDWVRQAPGKGLEWVGETRSKAFNYAT YYAESVKGRFTISRDDSKNSLYLQMNSLKTEDTAVYYCTPNWDEGFAYWGQGTLVTVSS (SEQ ID NO:141) and a light chain variable (VL) sequence of DVVMTQSPLSLPVTLGQPASISCRSSQSLVHSNGNTYLHWFQQRPGQSPRLLINKVSNRFSG VPDRFSGSGSGTDFTLKISRVEAEDVGVYYCSQSTHVPRTFGGGKVEIK (SEQ ID NO:146) for binding to COSMC knock-out T47D cells.

202. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of EVQLVESGGGLVQPGGSLRLSCAASGFTFSDAWMDWVRQAPGKGLEWVGETRSKAFNYAT YYAESVKGRFTISRDDSKNSLYLQMNSLKTEDTAVYYCTPNWDEGFAYWGQGTLVTVSS (SEQ ID NO:141) and a light chain variable (VL) sequence of DVVMTQSPLSLPVTLGQPASISCRSSQSLVHSNANVYLHWFQQRPGQSPRLLINKVSNRFSGV PDRFSGSGSGTDFTLKISRVEAEDVGVYYCSQSTHVPRTFGGGKVEIK (SEQ ID NO:147) for binding to COSMC knock-out T47D cells.

203. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of EVQLVESGGGLVQPGGSLRLSCAASGFTFSDAWMDWVRQAPGKGLEWVGETRSKAFNYAT YYAESVKGRFTISRDDSKNSLYLQMNSLKTEDTAVYYCTPNWDEGFAYWGQGTLVTVSS (SEQ ID NO:141) and a light chain variable (VL) sequence of DVVMTQSPDSLAVSLGERATINCRSSQSLVHSNGNTYLHWYQQKPGQPPKLLINKVSNRFSG VPDRFSGSGSGTDFTLTISSLQAEDVAVYFCSQSTHVPRTFGGGKVEIK (SEQ ID NO:148) for binding to COSMC knock-out T47D cells.

204. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of EVQLVESGGGLVQPGGSLRLSCAASGFTFSDAWMDWVRQAPGKGLEWVGETRSKAFNYATYYAESVKGRFTISRDDSKNSLYLQMNSLKTEDTAVYYCTPNWDEGFAYWGQGTLVTVSS (SEQ ID NO:141) and a light chain variable (VL) sequence of DVVMTQSPDSLAVSLGERATINCKSSQSLHNSGNTYLHWYQQKPGQPPKLLINKVSTRFSGVPDRFSGSGSGTDFTLTISLQAEDVAVYYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:149) for binding to COSMC knock-out T47D cells.

205. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of EVQLVESGGGLVQPGGSLRLSCAASGFTFSDAWMDWVRQAPGKGLEWVGETRSKAFNYATYYAESVKGRFTISRDDSKNSLYLQMNSLKTEDTAVYYCTPNWDEGFAYWGQGTLVTVSS (SEQ ID NO:141) and a light chain variable (VL) sequence of DVVMTQSPDSLAVSLGERATINCKSSQSLHNSNANVYLHWYQQKPGQPPKLLINKASTRESGV PDRFSGSGSGTDFTLTISLQAEDVAVYYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:150) for binding to COSMC knock-out T47D cells.

206. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of EVQLVESGGGLVQPGGSLRLSCAASGFTFSDAWMDWVRQAPGKGLEWVGETRSKAFNYATYYAESVKGRFTISRDDSKNSLYLQMNSLKTEDTAVYYCTPNWDEGFAYWGQGTLVTVSS (SEQ ID NO:141) and a light chain variable (VL) sequence of DVVMTQSPASLAVSPGQRATITCRSSQSLVHSNGNTYLHWYQQKPGQPPKLLINKVSNRFSGV PPARFSGSGSGTDFTLTINPVEANDTANYFCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:151) for binding to COSMC knock-out T47D cells.

207. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of EVQLVESGGGLVQPGGSLRLSCAASGFTFSDAWMDWVRQAPGKGLEWVGETRSKAFNYATYYAESVKGRFTISRDDSKNSLYLQMNSLKTEDTAVYYCTPNWDEGFAYWGQGTLVTVSS (SEQ ID NO:141) and a light chain variable (VL) sequence of DVVLTQSPASLAVSPGQRATITCRSSESLSHSNGNTYLHWYQQKPGQPPKLLINKVSNKFTGVPARFSGSGSGTDFTLTINPVEANDTANYYYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:152) for binding to COSMC knock-out T47D cells.

208. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody

or antigen binding fragment comprising a heavy chain variable (VH) sequence of EVQLVESGGGLVQPGGSLRLSCAASGFTFSDAWMDWVRQAPGKGLEWVGETRSKAFNYAT YYAESVKGRFTISRDDSKNSLYLQMNSLKTEDTAVYYCTPNWDEGFAYWGQGTLVTVSS (SEQ ID NO:141) and a light chain variable (VL) sequence of DVVLTQSPASLAVSPGQRATITCRASELSHSNANVYIHWYQQKPGQPPKLLINKASNKFTGV PARFSGSGSGTDFTLTINPVEANDTANYCYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:153) for binding to COSMC knock-out T47D cells.

209. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of QVQLVQSGSELKKPGASVKVSCASGFTFSDAWMDWVRHAPGQGLEWVAELRSKAFNHAT YYAESVKGRFVISRDDSVSTVYLQISSLKAEDTAVYYCTPNWDEGFAYWGQGTLVTVSS (SEQ ID NO:142) and a light chain variable (VL) sequence of DVVMTQSPLSLPVTLGQPASISCRSSQSLVHSNGNTYLHWYQQRPQGQSPRLLINKVSNRFSG VPDRFSGSGSGTDFTLKISRVEAEDVGVYFCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:145) for binding to COSMC knock-out T47D cells.

210. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of QVQLVQSGSELKKPGASVKVSCASGFTFSDAWMDWVRHAPGQGLEWVAELRSKAFNHAT YYAESVKGRFVISRDDSVSTVYLQISSLKAEDTAVYYCTPNWDEGFAYWGQGTLVTVSS (SEQ ID NO:142) and a light chain variable (VL) sequence of DVVMTQSPLSLPVTLGQPASISCRSSQSLVHSNGNTYLHWFQQRPQGQSPRLLINKVSNRFSG VPDRFSGSGSGTDFTLKISRVEAEDVGVYCYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:146) for binding to COSMC knock-out T47D cells.

211. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of QVQLVQSGSELKKPGASVKVSCASGFTFSDAWMDWVRHAPGQGLEWVAELRSKAFNHAT YYAESVKGRFVISRDDSVSTVYLQISSLKAEDTAVYYCTPNWDEGFAYWGQGTLVTVSS (SEQ ID NO:142) and a light chain variable (VL) sequence of DVVMTQSPLSLPVTLGQPASISCRSSQSLVHSNANVYLHWFQQRPQGQSPRLLINKVSNRFSGV PDRFSGSGSGTDFTLKISRVEAEDVGVYCYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:147) for binding to COSMC knock-out T47D cells.

212. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of QVQLVQSGSELKKPGASVKVSCASGFTFSDAWMDWVRHAPGQGLEWVAELRSKAFNHAT

YYAESVKGRFVISRDDSVSTVYLQISSLKAEDTAVYYCTPNWDEGFAYWGQGLTVTVSS (SEQ ID NO:142) and a light chain variable (VL) sequence of DVVMTQSPDSLAVSLGERATINCRSSQSLVHSNGNTYLHWYQQKPGQPPKLLINKVSNRFSGVPDRFSGSGSGTDFTLTISLQAEDVAVYFCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:148) for binding to COSMC knock-out T47D cells.

213. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of QVQLVQSGSELKKPGASVKVSCASGFTFSDAWMDWVRHAPGQGLEWVAELRSKAFNHATYYAESVKGRFVISRDDSVSTVYLQISSLKAEDTAVYYCTPNWDEGFAYWGQGLTVTVSS (SEQ ID NO:142) and a light chain variable (VL) sequence of DVVMTQSPDSLAVSLGERATINCKSSQSLLSHNGNTYLHWYQQKPGQPPKLLINKVSTRFSGVPDRFSGSGSGTDFTLTISLQAEDVAVYYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:149) for binding to COSMC knock-out T47D cells.

214. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of QVQLVQSGSELKKPGASVKVSCASGFTFSDAWMDWVRHAPGQGLEWVAELRSKAFNHATYYAESVKGRFVISRDDSVSTVYLQISSLKAEDTAVYYCTPNWDEGFAYWGQGLTVTVSS (SEQ ID NO:142) and a light chain variable (VL) sequence of DVVMTQSPDSLAVSLGERATINCKSSQSLLSHNSANVYLHWYQQKPGQPPKLLINKASTRESGVVPDRFSGSGSGTDFTLTISLQAEDVAVYYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:150) for binding to COSMC knock-out T47D cells.

215. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of QVQLVQSGSELKKPGASVKVSCASGFTFSDAWMDWVRHAPGQGLEWVAELRSKAFNHATYYAESVKGRFVISRDDSVSTVYLQISSLKAEDTAVYYCTPNWDEGFAYWGQGLTVTVSS (SEQ ID NO:142) and a light chain variable (VL) sequence of DVVMTQSPASLAVSPGQRATITCRSSQSLVHSNGNTYLHWYQQKPGQPPKLLINKVSNRFSGVPARFSGSGSGTDFTLTINPVEANDTANYFCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:151) for binding to COSMC knock-out T47D cells.

216. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of QVQLVQSGSELKKPGASVKVSCASGFTFSDAWMDWVRHAPGQGLEWVAELRSKAFNHATYYAESVKGRFVISRDDSVSTVYLQISSLKAEDTAVYYCTPNWDEGFAYWGQGLTVTVSS (SEQ ID NO:142) and a light chain variable (VL) sequence of

DVVLTSQSPASLAVSPGQRATITCRSSESLSHSNGNTYLHWYQQKPGQPPKLLINKVSNKFTGV
PARFSGSGSGTDFTLTINPVEANDTANYCYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:152) for
binding to COSMC knock-out T47D cells.

217. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124,
wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody
or antigen binding fragment comprising a heavy chain variable (VH) sequence of
QVQLVQSGSELKKPGASVKVSCASGFTFSDAWMDWVRHAPGQGLEWVAELRSKAFNHAT
YYAESVKGRFVISRDDSVSTVYLQISSLKAEDTAVYYCTPNWDEGFAYWGQGLTVTVSS (SEQ
ID NO:142) and a light chain variable (VL) sequence of
DVVLTSQSPASLAVSPGQRATITCRASESLSHSNANVYIHWYQQKPGQPPKLLINKASNKFTGV
PARFSGSGSGTDFTLTINPVEANDTANYCYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:153) for
binding to COSMC knock-out T47D cells.

218. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124,
wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody
or antigen binding fragment comprising a heavy chain variable (VH) sequence of
QVQLVQSGSELKKPGASVKVSCASGYTFSDAWMDWVRQAPGQGLEWMGELRSKAFNHAT
YYAESVKGRFVISRDDSVSTAYLQISSLKAEDTAVYYCAPNWDEGFAYWGQGLTVTVSS (SEQ
ID NO:143) and a light chain variable (VL) sequence of
DVVMTQSPLSLPVTLGQPASISCRSSQSLVHSNGNTYLHWYQQRPGQSPRLLINKVSNRFSG
VPDRFSGSGSGTDFTLKISRVEAEDVGVYFCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:145)
for binding to COSMC knock-out T47D cells.

219. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124,
wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody
or antigen binding fragment comprising a heavy chain variable (VH) sequence of
QVQLVQSGSELKKPGASVKVSCASGYTFSDAWMDWVRQAPGQGLEWMGELRSKAFNHAT
YYAESVKGRFVISRDDSVSTAYLQISSLKAEDTAVYYCAPNWDEGFAYWGQGLTVTVSS (SEQ
ID NO:143) and a light chain variable (VL) sequence of
DVVMTQSPLSLPVTLGQPASISCRSSQSLVHSNGNTYLHWFQQRPGQSPRLLINKVSNRFSG
VPDRFSGSGSGTDFTLKISRVEAEDVGVYCYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:146)
for binding to COSMC knock-out T47D cells.

220. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124,
wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody
or antigen binding fragment comprising a heavy chain variable (VH) sequence of
QVQLVQSGSELKKPGASVKVSCASGYTFSDAWMDWVRQAPGQGLEWMGELRSKAFNHAT
YYAESVKGRFVISRDDSVSTAYLQISSLKAEDTAVYYCAPNWDEGFAYWGQGLTVTVSS (SEQ
ID NO:143) and a light chain variable (VL) sequence of
DVVMTQSPLSLPVTLGQPASISCRSSQSLVHSNANVYLHWFQQRPGQSPRLLINKVSNRFSGV

PDRFSGSGSGTDFTLKISRVEAEDVGVYYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:147) for binding to COSMC knock-out T47D cells.

221. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of QVQLVQSGSELKKPGASVKVSCASGYTFSDAWMDWVRQAPGQGLEWMGELRSKAFNHAT YYAESVKGRFVISRDDSVSTAYLQISSLKAEDTAVYYCAPNWDEGFAYWGQGLTVTVSS (SEQ ID NO:143) and a light chain variable (VL) sequence of DVVMTQSPDSLAVSLGERATINCRSSQSLVHSNGNTYLHWYQQKPGQPPKLLINKVSNRFSG VPDRFSGSGSGTDFTLTISLQAEDVAVYFCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:148) for binding to COSMC knock-out T47D cells.

222. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of QVQLVQSGSELKKPGASVKVSCASGYTFSDAWMDWVRQAPGQGLEWMGELRSKAFNHAT YYAESVKGRFVISRDDSVSTAYLQISSLKAEDTAVYYCAPNWDEGFAYWGQGLTVTVSS (SEQ ID NO:143) and a light chain variable (VL) sequence of DVVMTQSPDSLAVSLGERATINCKSSQSLLSNGNTYLHWYQQKPGQPPKLLINKVSTRFSGV PDRFSGSGSGTDFTLTISLQAEDVAVYYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:149) for binding to COSMC knock-out T47D cells.

223. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of QVQLVQSGSELKKPGASVKVSCASGYTFSDAWMDWVRQAPGQGLEWMGELRSKAFNHAT YYAESVKGRFVISRDDSVSTAYLQISSLKAEDTAVYYCAPNWDEGFAYWGQGLTVTVSS (SEQ ID NO:143) and a light chain variable (VL) sequence of DVVMTQSPDSLAVSLGERATINCKSSQSLLSNANVYLHWYQQKPGQPPKLLINKASTRESGV PDRFSGSGSGTDFTLTISLQAEDVAVYYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:150) for binding to COSMC knock-out T47D cells.

224. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of QVQLVQSGSELKKPGASVKVSCASGYTFSDAWMDWVRQAPGQGLEWMGELRSKAFNHAT YYAESVKGRFVISRDDSVSTAYLQISSLKAEDTAVYYCAPNWDEGFAYWGQGLTVTVSS (SEQ ID NO:143) and a light chain variable (VL) sequence of DVVMTQSPASLAVSPGQRATITCRSSQSLVHSNGNTYLHWYQQKPGQPPKLLINKVSNRFSG VPARFSGSGSGTDFTLTINPVEANDTANYFCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:151) for binding to COSMC knock-out T47D cells.

225. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of QVQLVQSGSELKKPGASVKVSCKASGYTFSDAWMDWVRQAPGQGLEWMGELRSKAFNHAT YYAESVKGRFVISRDDSVSTAYLQISSLKAEDTAVYYCAPNWDEGFAYWGQGLTVTVSS (SEQ ID NO:143) and a light chain variable (VL) sequence of DVVLTQSPASLAVSPGQRATITCRSSESLSHSNGNTYLHWYQQKPGQPPKLLINKVSNKFTGV PARFSGSGSGTDFTLTINPVEANDTANYYYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:152) for binding to COSMC knock-out T47D cells.

226. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of QVQLVQSGSELKKPGASVKVSCKASGYTFSDAWMDWVRQAPGQGLEWMGELRSKAFNHAT YYAESVKGRFVISRDDSVSTAYLQISSLKAEDTAVYYCAPNWDEGFAYWGQGLTVTVSS (SEQ ID NO:143) and a light chain variable (VL) sequence of DVVLTQSPASLAVSPGQRATITCRASESLSHSNANVYIHWYQQKPGQPPKLLINKASNKFTGV PARFSGSGSGTDFTLTINPVEANDTANYYYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:153) for binding to COSMC knock-out T47D cells.

227. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of QVQLVQSGSELKKPGASVKVSCKASGYTFTSAWMNWVRQAPGQGLEWMGEIRTNAFNHAP YYAQGVKGRFVISRDDSVSTAYLQISSLKAEDTAVYYCAPNWDEGFAYWGQGLTVTVSS (SEQ ID NO:144) and a light chain variable (VL) sequence of DVVMTQSPLSLPVTLGQPASISCRSSQSLVHSNGNTYLHWYQQRPGQSPRLLINKVSNRFSG VPDRFSGSGSGTDFTLKISRVEAEDVGVYFCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:145) for binding to COSMC knock-out T47D cells.

228. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of QVQLVQSGSELKKPGASVKVSCKASGYTFTSAWMNWVRQAPGQGLEWMGEIRTNAFNHAP YYAQGVKGRFVISRDDSVSTAYLQISSLKAEDTAVYYCAPNWDEGFAYWGQGLTVTVSS (SEQ ID NO:144) and a light chain variable (VL) sequence of DVVMTQSPLSLPVTLGQPASISCRSSQSLVHSNGNTYLHWFQQRPGQSPRLLINKVSNRFSG VPDRFSGSGSGTDFTLKISRVEAEDVGVYYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:146) for binding to COSMC knock-out T47D cells.

229. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody

or antigen binding fragment comprising a heavy chain variable (VH) sequence of QVQLVQSGSELKKPGASVKVSCASGYTFTSAWMNWRQAPGQGLEWMGEIRTNAFNHAP YYAQGVKGRFVISRDDSVSTAYLQISLKAEDTAVYYCAPNWDEGFAYWGQGTLLTVSS (SEQ ID NO:144) and a light chain variable (VL) sequence of DVVMTQSPSLPVTLGQPASISCRSSQSLVHSNANVYLHWYFQQRPQGSPRLLINKVSNRFGSGV PDRFSGSGSGTDFTLKISRVEAEDVGVYYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:147) for binding to COSMC knock-out T47D cells.

230. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of QVQLVQSGSELKKPGASVKVSCASGYTFTSAWMNWRQAPGQGLEWMGEIRTNAFNHAP YYAQGVKGRFVISRDDSVSTAYLQISLKAEDTAVYYCAPNWDEGFAYWGQGTLLTVSS (SEQ ID NO:144) and a light chain variable (VL) sequence of DVVMTQSPDSLAVSLGERATINCRSSQSLVHSNGNTYLHWYQQKPGQPPKLLINKVSNRFGSG VPDRFSGSGSGTDFTLTISLQAEDVAVYFCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:148) for binding to COSMC knock-out T47D cells.

231. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of QVQLVQSGSELKKPGASVKVSCASGYTFTSAWMNWRQAPGQGLEWMGEIRTNAFNHAP YYAQGVKGRFVISRDDSVSTAYLQISLKAEDTAVYYCAPNWDEGFAYWGQGTLLTVSS (SEQ ID NO:144) and a light chain variable (VL) sequence of DVVMTQSPDSLAVSLGERATINCKSSQSLLSNNGNTYLHWYQQKPGQPPKLLINKVSTRFGSGV PDRFSGSGSGTDFTLTISLQAEDVAVYYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:149) for binding to COSMC knock-out T47D cells.

232. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of QVQLVQSGSELKKPGASVKVSCASGYTFTSAWMNWRQAPGQGLEWMGEIRTNAFNHAP YYAQGVKGRFVISRDDSVSTAYLQISLKAEDTAVYYCAPNWDEGFAYWGQGTLLTVSS (SEQ ID NO:144) and a light chain variable (VL) sequence of DVVMTQSPDSLAVSLGERATINCKSSQSLLSNANVYLHWYQQKPGQPPKLLINKASTRESGV PDRFSGSGSGTDFTLTISLQAEDVAVYYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:150) for binding to COSMC knock-out T47D cells.

233. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of QVQLVQSGSELKKPGASVKVSCASGYTFTSAWMNWRQAPGQGLEWMGEIRTNAFNHAP

YYAQGVKGRFVISRDDSVSTAYLQISSLKAEDTAVYYCAPNWDEGFAYWGQGLTVTVSS
(SEQ ID NO:144) and a light chain variable (VL) sequence of
DVVMTQSPASLAVSPGQRATITCRSSQSLVHSNGNTYLHWYQQKPGQPPKLLINKVSNRFSG
VPAFSGSGSGTDFTLTINPVEANDTANYFCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:151)
for binding to COSMC knock-out T47D cells.

234. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of
QVQLVQSGSELKKPGASVKVSCASGYTFTSAWMNWRQAPGQGLEWMGEIRTNFAFNHAP
YYAQGVKGRFVISRDDSVSTAYLQISSLKAEDTAVYYCAPNWDEGFAYWGQGLTVTVSS
(SEQ ID NO:144) and a light chain variable (VL) sequence of
DVVLTQSPASLAVSPGQRATITCRSSQSLVHSNGNTYLHWYQQKPGQPPKLLINKVSNKFTGV
PARFSGSGSGTDFTLTINPVEANDTANYFCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:152) for binding to COSMC knock-out T47D cells.

235. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 124, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of
QVQLVQSGSELKKPGASVKVSCASGYTFTSAWMNWRQAPGQGLEWMGEIRTNFAFNHAP
YYAQGVKGRFVISRDDSVSTAYLQISSLKAEDTAVYYCAPNWDEGFAYWGQGLTVTVSS
(SEQ ID NO:144) and a light chain variable (VL) sequence of
DVVLTQSPASLAVSPGQRATITCRASESLSHSNANVYIHWYQQKPGQPPKLLINKASNKFTGV
PARFSGSGSGTDFTLTINPVEANDTANYFCSQSTHVPRTFGGGTKVEIK (SEQ ID NO:153) for binding to COSMC knock-out T47D cells.

236. An anti-glyco-LAMP1 antibody or antigen-binding fragment, which is optionally an anti-glyco-LAMP1 antibody or antigen-binding fragment according to any one of embodiments 1 to 235, comprising:

- (a) a complementarity determining region (CDR) H1 comprising the amino acid sequence of a CDR-H1 of any one of Tables 1D, 1E, 1F, 2D, and 3D (e.g., SEQ ID NO:67, SEQ ID NO:73, SEQ ID NO:79, SEQ ID NO:103, or SEQ ID NO:127);
- (b) a CDR-H2 comprising the amino acid sequence of a CDR-H2 of any one of Tables 1D, 1E, 1F, 2D, and 3D (e.g., SEQ ID NO:68, SEQ ID NO:74, SEQ ID NO:80, SEQ ID NO:104, or SEQ ID NO:128);
- (c) a CDR-H3 comprising the amino acid sequence of a CDR-H3 of any one of Tables 1D, 1E, 1F, 2D, and 3D (e.g., SEQ ID NO:69, SEQ ID NO: 75, SEQ ID NO: 81, SEQ ID NO:105, or SEQ ID NO:129);

- (d) a CDR-L1 comprising the amino acid sequence of a CDR-L1 of any one of Tables 1D, 1E, 1F, 2D, and 3D (e.g., SEQ ID NO:70, SEQ ID NO:76, SEQ ID NO:82, SEQ ID NO:106, or SEQ ID NO:130);
- (e) a CDR-L2 comprising the amino acid sequence of a CDR-L2 of any one of Tables 1D, 1E, 1F, 2D, and 3D (e.g., SEQ ID NO:71, SEQ ID NO:77, SEQ ID NO:83, SEQ ID NO:107, or SEQ ID NO:131); and
- (f) a CDR-L3 comprising the amino acid sequence of a CDR-L3 of any one of Tables 1D, 1E, 1F, 2D, and 3D (e.g., SEQ ID NO:72, SEQ ID NO:78, SEQ ID NO:84, SEQ ID NO:108, or SEQ ID NO:132).

237. The anti-glyco-LAMP1 antibody or antigen-binding fragment of embodiment 236, wherein the amino acid designated X_1 in a CDR sequence of any one of Tables 1D, 1E, 1F, 2D, and 3D (e.g., SEQ ID NO:68, SEQ ID NO:74, and/or SEQ ID NO:104) is L.

238. The anti-glyco-LAMP1 antibody or antigen-binding fragment of embodiment 236, wherein the amino acid designated X_1 in a CDR sequence of any one of Tables 1D, 1E, 1F, 2D, and 3D (e.g., SEQ ID NO:68, SEQ ID NO:74, and/or SEQ ID NO:104) is M.

239. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 236 to 238, wherein the amino acid designated X_2 in a CDR sequence of any one of Tables 1D, 1E, 1F, 2D, and 3D (e.g., SEQ ID NO:68, SEQ ID NO:74, SEQ ID NO:80, SEQ ID NO:104, and/or SEQ ID NO:128) is A.

240. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 236 to 238, wherein the amino acid designated X_2 in a CDR sequence of any one of Tables 1D, 1E, 1F, 2D, and 3D (e.g., SEQ ID NO:68, SEQ ID NO:74, SEQ ID NO:80, SEQ ID NO:104, and/or SEQ ID NO:128) is M.

241. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 236 to 240, wherein the amino acid designated X_3 in a CDR sequence of any one of Tables 1D, 1E, 1F, 2D, and 3D (e.g., SEQ ID NO:68, SEQ ID NO:74 and/or SEQ ID NO:104) is T.

242. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 236 to 240, wherein the amino acid designated X_3 in a CDR sequence of any one of Tables 1D, 1E, 1F, 2D, and 3D (e.g., SEQ ID NO:68, SEQ ID NO:74 and/or SEQ ID NO:104) is I.

243. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 236 to 242, wherein the amino acid designated X_4 in a CDR sequence of any one of Tables 1D, 1E, 1F, 2D, and 3D (e.g., SEQ ID NO:74 and/or SEQ ID NO:104) is K.

244. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 236 to 242, wherein the amino acid designated X_4 in a CDR sequence of any one of Tables 1D, 1E, 1F, 2D, and 3D (e.g., SEQ ID NO:74 and/or SEQ ID NO:104) is R.

245. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 236 to 244, wherein the amino acid designated X₅ in a CDR sequence of any one of Tables 1D, 1E, 1F, 2D, and 3D (e.g., SEQ ID NO:69 and/or SEQ ID NO:105) is T.

246. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 236 to 244, wherein the amino acid designated X₅ in a CDR sequence of any one of Tables 1D, 1E, 1F, 2D, and 3D (e.g., SEQ ID NO:69 and/or SEQ ID NO:105) is S.

247. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 236 to 244, wherein the amino acid designated X₆ in a CDR sequence of any one of Tables 1D, 1E, 1F, 2D, and 3D (e.g., SEQ ID NO:70, SEQ ID NO: 76, SEQ ID NO: 82, SEQ ID NO:106, and/or SEQ ID NO:130) is S.

248. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 236 to 244, wherein the amino acid designated X₆ in a CDR sequence of any one of Tables 1D, 1E, 1F, 2D, and 3D (e.g., SEQ ID NO:70, SEQ ID NO: 76, SEQ ID NO: 82, SEQ ID NO:106, and/or SEQ ID NO:130) is N.

249. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 236 to 248, wherein the amino acid designated X₇ in a CDR sequence of any one of Tables 1D, 1E, 1F, 2D, and 3D (e.g., SEQ ID NO:77, SEQ ID NO:83, and/or SEQ ID NO:107) is N.

250. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 236 to 248, wherein the amino acid designated X₇ in a CDR sequence of any one of Tables 1D, 1E, 1F, 2D, and 3D (e.g., SEQ ID NO:77, SEQ ID NO:83, and/or SEQ ID NO:107) is K.

251. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 236 to 250, wherein the amino acid designated X₈ in a CDR sequence of any one of Tables 1D, 1E, 1F, 2D, and 3D (e.g., SEQ ID NO:77, SEQ ID NO:83, and/or SEQ ID NO:107) is S.

252. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 236 to 250, wherein the amino acid designated X₈ in a CDR sequence of any one of Tables 1D, 1E, 1F, 2D, and 3D (e.g., SEQ ID NO:77, SEQ ID NO:83, and/or SEQ ID NO:107) is F.

253. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 236 to 252, wherein CDR-H1 comprises the amino acid sequence of GFTFSDAW (SEQ ID NO:67).

254. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 236 to 252, wherein CDR-H1 comprises the amino acid sequence of DAWMD (SEQ ID NO:73).

255. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 236 to 252, wherein CDR-H1 comprises the amino acid sequence of GFTFSDA (SEQ ID NO:79).

256. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 236 to 252, wherein CDR-H1 comprises the amino acid sequence of GFTFSDAWMD (SEQ ID NO:103).

257. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 236 to 252, wherein CDR-H1 comprises the amino acid sequence of DA (SEQ ID NO:127).

258. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 236 to 257, wherein CDR-H2 comprises the amino acid sequence of X₁RSKX₂FNHAX₃ (SEQ ID NO:68).

259. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 236 to 257, wherein CDR-H2 comprises the amino acid sequence of EX₁RSKX₂FNHAX₃YYAESVX₄G (SEQ ID NO:74).

260. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 236 to 257, wherein CDR-H2 comprises the amino acid sequence of RSKX₂FNHA (SEQ ID NO:80).

261. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 236 to 257, wherein CDR-H2 comprises the amino acid sequence of EX₁RSKX₂FNHAX₃YYAESVX₄G (SEQ ID NO:104).

262. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 236 to 257, wherein CDR-H2 comprises the amino acid sequence of SKX₂FNHA (SEQ ID NO:128).

263. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 236 to 262, wherein CDR-H3 comprises the amino acid sequence of X₅PNWDEGFAY (SEQ ID NO:69).

264. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 236 to 262, wherein CDR-H3 comprises the amino acid sequence of NWDEGFAY (SEQ ID NO: 75).

265. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 236 to 262, wherein CDR-H3 comprises the amino acid sequence of NWDEGFAY (SEQ ID NO:81).

266. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 236 to 262, wherein CDR-H3 comprises the amino acid sequence of X₅PNWDEGFAY (SEQ ID NO:105).

267. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 236 to 262, wherein CDR-H3 comprises the amino acid sequence of NWDEGFAY (SEQ ID NO:129).

268. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 236 to 267, wherein CDR-L1 comprises the amino acid sequence of QSLVHX₆NGNTY (SEQ ID NO:70).

269. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 236 to 267, wherein CDR-L1 comprises the amino acid sequence of RSSQSLVHX₆NGNTYLH (SEQ ID NO:76).

270. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 236 to 267, wherein CDR-L1 comprises the amino acid sequence of RSSQSLVHX₆NGNTYLH (SEQ ID NO:82).

271. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 236 to 267, wherein CDR-L1 comprises the amino acid sequence of RSSQSLVHX₆NGNTYLH (SEQ ID NO:106).

272. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 236 to 267, wherein CDR-L1 comprises the amino acid sequence of QSLVHX₆NGNTY (SEQ ID NO:130).

273. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 236 to 272, wherein CDR-L2 comprises the amino acid sequence of KVS (SEQ ID NO:71).

274. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 236 to 272, wherein CDR-L2 comprises the amino acid sequence of KVSX₇RFX₈ (SEQ ID NO:77).

275. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 236 to 272, wherein CDR-L2 comprises the amino acid sequence of KVSX₇RFX₈ (SEQ ID NO:83).

276. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 236 to 272, wherein CDR-L2 comprises the amino acid sequence of KVSX₇RFX₈ (SEQ ID NO:107).

277. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 236 to 272, wherein CDR-L2 comprises the amino acid sequence of KVS (SEQ ID NO:131).

278. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 236 to 277, wherein CDR-L3 comprises the amino acid sequence of SQSTHVPRT (SEQ ID NO:72).

279. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 236 to 277, wherein CDR-L3 comprises the amino acid sequence of SQSTHVPRT (SEQ ID NO:78).

280. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 236 to 277, wherein CDR-L3 comprises the amino acid sequence of SQSTHVPRT (SEQ ID NO:84).

281. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 236 to 277, wherein CDR-L3 comprises the amino acid sequence of SQSTHVPRT (SEQ ID NO:108).

282. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 236 to 277, wherein CDR-L3 comprises the amino acid sequence of HQYLSSYT (SEQ ID NO:132).

283. An anti-glyco-LAMP1 antibody or antigen-binding fragment, which is optionally an anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 1 to 235, which comprises a VH comprising CDRs of 3C7 as defined by IMGT (*e.g.*, SEQ ID NOS:3-5) and a VL comprising CDRs of 3C7 as defined by IMGT (*e.g.*, SEQ ID NOS:6-8).

284. An anti-glyco-LAMP1 antibody or antigen-binding fragment, which is optionally an anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 1 to 235, which comprises a VH comprising CDRs of 3C7 as defined by Kabat (*e.g.*, SEQ ID NOS:9-11) and a VL comprising CDRs of 3C7 as defined by Kabat (*e.g.*, SEQ ID NOS:12-14).

285. An anti-glyco-LAMP1 antibody or antigen-binding fragment, which is optionally an anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 1 to 235, which comprises a VH comprising CDRs of 3C7 as defined by Chothia (*e.g.*, SEQ ID NOS:15-17) and a VL comprising CDRs of 3C7 as defined by Chothia (*e.g.*, SEQ ID NOS:18-20).

286. An anti-glyco-LAMP1 antibody or antigen-binding fragment, which is optionally an anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 1 to 235, which comprises a VH comprising CDRs of 13C3 as defined by IMGT (*e.g.*, SEQ ID NOS:25-27) and a VL comprising CDRs of 13C3 as defined by IMGT (*e.g.*, SEQ ID NOS:28-30).

287. An anti-glyco-LAMP1 antibody or antigen-binding fragment, which is optionally an anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 1 to 235, which comprises a VH comprising CDRs of 13C3 as defined by Kabat (*e.g.*, SEQ ID NOS:31-33) and a VL comprising CDRs of 13C3 as defined by Kabat (*e.g.*, SEQ ID NOS:34-36).

288. An anti-glyco-LAMP1 antibody or antigen-binding fragment, which is optionally an anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 1 to 235, which comprises a VH comprising CDRs of 13C3 as defined by Chothia (*e.g.*, SEQ ID

NOS:37-39) and a VL comprising CDRs of 13C3 as defined by Chothia (*e.g.*, SEQ ID NOS:40-42).

289. An anti-glyco-LAMP1 antibody or antigen-binding fragment, which is optionally an anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 1 to 235, which comprises a VH comprising CDRs of 13G2 as defined by IMGT (*e.g.*, SEQ ID NOS:47-49) and a VL comprising CDRs of 13G2 as defined by IMGT (*e.g.*, SEQ ID NOS:50-52).

290. An anti-glyco-LAMP1 antibody or antigen-binding fragment, which is optionally an anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 1 to 235, which comprises a VH comprising CDRs of 13G2 as defined by Kabat (*e.g.*, SEQ ID NOS:53-55) and a VL comprising CDRs of 13G2 as defined by Kabat (*e.g.*, SEQ ID NOS:56-58).

291. An anti-glyco-LAMP1 antibody or antigen-binding fragment, which is optionally an anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 1 to 235, which comprises a VH comprising CDRs of 13G2 as defined by Chothia (*e.g.*, SEQ ID NOS:59-61) and a VL comprising CDRs of 13G2 as defined by Chothia (*e.g.*, SEQ ID NOS:62-64).

292. An anti-glyco-LAMP1 antibody or antigen-binding fragment, which is optionally an anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 1 to 235, which comprises a VH comprising CDRs of GFTFSDAWMD (SEQ ID NO:85), EMRSKAFNHAIYYAESVKG (SEQ ID NO:86), and TPNWDEGFAY (SEQ ID NO:87); and a VL comprising CDRs of RSSQSLVHSNGNTYLH (SEQ ID NO:88), KVSNRFF (SEQ ID NO:89), and SQSTHVPRT (SEQ ID NO:90).

293. An anti-glyco-LAMP1 antibody or antigen-binding fragment, which is optionally an anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 1 to 235, which comprises a VH comprising CDRs of GFTFSDAWMD (SEQ ID NO:91), ELRSKAFNHATYYAESVKG (SEQ ID NO:92), and TPNWDEGFAY (SEQ ID NO:93); and a VL comprising CDRs of RSSQSLVHSNGNTYLH (SEQ ID NO:94), KVSNRFS (SEQ ID NO:95), and SQSTHVPRT (SEQ ID NO: 96).

294. An anti-glyco-LAMP1 antibody or antigen-binding fragment, which is optionally an anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 1 to 235, which comprises a VH comprising CDRs of GFTFSDAWMD (SEQ ID NO:97), ELRSKTFNHATYYAESVRG (SEQ ID NO:98), and SPNWDEGFAY (SEQ ID NO:99); and a VL comprising CDRs of RSSQSLVHNNNGNTYLH (SEQ ID NO:100), KVSKRFT (SEQ ID NO:101), and SQSTHVPRT (SEQ ID NO:102).

295. An anti-glyco-LAMP1 antibody or antigen-binding fragment, which is optionally an anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 1 to 235, which comprises a VH comprising CDRs of DA (SEQ ID NO:109), RSKAFNHA (SEQ ID

NO: 110), and NWDEGFAY (SEQ ID NO:111); and a VL comprising CDRs of QSLVHSNGNTY (SEQ ID NO:112), KVS (SEQ ID NO:113), and SQSTHVPRT (SEQ ID NO:114).

296. An anti-glyco-LAMP1 antibody or antigen-binding fragment, which is optionally an anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 1 to 235, which comprises a VH comprising CDRs of DA (SEQ ID NO:115), RSKAFNHA (SEQ ID NO: 116), and NWDEGFAY (SEQ ID NO:117); and a VL comprising CDRs of QSLVHSNGNTY (SEQ ID NO:118), KVS (SEQ ID NO:119), and SQSTHVPRT (SEQ ID NO:120).

297. An anti-glyco-LAMP1 antibody or antigen-binding fragment, which is optionally an anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 1 to 235, which comprises a VH comprising CDRs of DA (SEQ ID NO:121), RSKTFNHA (SEQ ID NO: 122), and NWDEGFAY (SEQ ID NO:123); and a VL comprising CDRs of QSLVHNNGNTY (SEQ ID NO:124), KVS (SEQ ID NO:125), and SQSTHVPRT (SEQ ID NO:126).

298. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 1 to 297, which is a chimeric or humanized antibody or antigen-binding fragment of a chimeric or humanized antibody.

299. An anti-glyco-LAMP1 antibody or antigen-binding fragment, which is optionally anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 1 to 298, which comprises a VH comprising an amino acid sequence having at least 95% sequence identity to

EVKLEESGGGLVQPGGSMKVSCGASGFTFSDAWMDWVRQSPEKGLEWVAEMRSKAFNHAI
YYAESVKGRFTISRDDSKSRVYLQMNLLRPEDTGIYYCTPNWDEGFAYWGQGTTLTVSA
(SEQ ID NO:1) and a VL comprising an amino acid sequence having at least 95% sequence identity to

DVMLTQTPLSLPVSLGDQASISCRSSQSLVHSNGNTYLHWYLQKPGQSPKLLINKVSNRFFGV
PDRFSGSGSGTDFTLKISRVEAEDLGVYFCSQSTHVPRTFGGGTKLEIK (SEQ ID NO:2).

300. An anti-glyco-LAMP1 antibody or antigen-binding fragment, which is optionally an anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 1 to 299, which comprises a VH comprising an amino acid sequence having at least 97% sequence identity to

EVKLEESGGGLVQPGGSMKVSCGASGFTFSDAWMDWVRQSPEKGLEWVAEMRSKAFNHAI
YYAESVKGRFTISRDDSKSRVYLQMNLLRPEDTGIYYCTPNWDEGFAYWGQGTTLTVSA
(SEQ ID NO:1) and a VL comprising an amino acid sequence having at least 97% sequence identity to

DVMLTQTPLSLPVSLGDQASISCRSSQSLVHSNGNTYLHWYLQKPGQSPKLLINKVSNRFFGV
PDRFSGSGSGTDFTLKISRVEAEDLGVYFCSQSTHVPRTFGGGTKLEIK (SEQ ID NO:2).

301. An anti-glyco-LAMP1 antibody or antigen-binding fragment, which is optionally an anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 1 to 300, which comprises a VH comprising an amino acid sequence having at least 99% sequence

identity to

EVKLEESGGGLVQPGGSMKVSCGASGFTFSDAWMDWVRQSPEKGLEWVAEMRSKAFNHAI
YYAESVKGRFTISRDDSKSRVYLQMNLLRPEDTGIYYCTPNWDEGFAYWGQGTTLTVSA
(SEQ ID NO:1) and a VL comprising an amino acid sequence having at least 99% sequence
identity to

DVMLTQTPLSLPVSLGDQASISCRSSQSLVHSNGNTYLHWYLQKPGQSPKLLINKVSNRFFGV
PDRFSGSGSGTDFTLKISRVEAEDLGVYFCSQSTHVPRTFGGGTKLEIK (SEQ ID NO:2).

302. An anti-glyco-LAMP1 antibody or antigen-binding fragment, which is optionally
an anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 1 to
301, which comprises a VH comprising the amino acid sequence of

EVKLEESGGGLVQPGGSMKVSCGASGFTFSDAWMDWVRQSPEKGLEWVAEMRSKAFNHAI
YYAESVKGRFTISRDDSKSRVYLQMNLLRPEDTGIYYCTPNWDEGFAYWGQGTTLTVSA
(SEQ ID NO:1) and a VL comprising the amino acid sequence of

DVMLTQTPLSLPVSLGDQASISCRSSQSLVHSNGNTYLHWYLQKPGQSPKLLINKVSNRFFGV
PDRFSGSGSGTDFTLKISRVEAEDLGVYFCSQSTHVPRTFGGGTKLEIK (SEQ ID NO:2).

303. An anti-glyco-LAMP1 antibody or antigen-binding fragment, which is optionally
an anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 1 to
298, which comprises a VH comprising an amino acid sequence having at least 95% sequence
identity to

EVKLEDSGGGLVQPGGSMKLSCAASGFTFSDAWMDWVRHSPEKGLEWVAELRSKAFNHAT
YYAESVKGRFTISRDDSKSTVYLQMNSLRAEDTGIYYCTPNWDEGFAYWGQGTTLTVSA
(SEQ ID NO:23) and a VL comprising an amino acid sequence having at least 95% sequence
identity to

NIMMTQSPSSLVVSAGEKVTMSCKSSHSVLYSSNQKNYLAWYQQKPGQSPKLLIWASTKNS
GVPDRFTGSGSGTDFTLTISVQAEDLAVYYCHQYLSSYTFGGGTKEIK (SEQ ID NO:24).

304. An anti-glyco-LAMP1 antibody or antigen-binding fragment, which is optionally
an anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 1 to 298
or 303, which comprises a VH comprising an amino acid sequence having at least 97%
sequence identity to

EVKLEDSGGGLVQPGGSMKLSCAASGFTFSDAWMDWVRHSPEKGLEWVAELRSKAFNHAT
YYAESVKGRFTISRDDSKSTVYLQMNSLRAEDTGIYYCTPNWDEGFAYWGQGTTLTVSA
(SEQ ID NO:23) and a VL comprising an amino acid sequence having at least 97% sequence
identity to

NIMMTQSPSSLVVSAGEKVTMSCKSSHSVLYSSNQKNYLAWYQQKPGQSPKLLIWASTKNS
GVPDRFTGSGSGTDFTLTISVQAEDLAVYYCHQYLSSYTFGGGTKEIK (SEQ ID NO:24).

305. An anti-glyco-LAMP1 antibody or antigen-binding fragment, which is optionally
an anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 1 to
298, 303, or 304, which comprises a VH comprising an amino acid sequence having at least

99% sequence identity to

EVKLEDSGGGLVQPGGSMKLSCAASGFTFSDAWMDWVRHSPEKGLEWVAELRSKAFNHAT
YYAESVKGRFTISRDDSKSTVYLMNSLRAEDTGIYYCTPNWDEGFAYWGQGTTLTVSA
(SEQ ID NO:23) and a VL comprising an amino acid sequence having at least 99% sequence
identity to

NIMMTQSPSSLVVSAGEKVTMSCKSSHSVLYSSNQKNYLAWYQQKPGQSPKLLIWASTKNS
GVPDRFTGSGSGTDFTLTISVQAEDLAVYYCHQYLSSYTFGGGTKLEIK (SEQ ID NO:24).

306. An anti-glyco-LAMP1 antibody or antigen-binding fragment, which is optionally
an anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 1 to 298
or 303 to 305, which comprises a VH comprising the amino acid sequence of

EVKLEDSGGGLVQPGGSMKLSCAASGFTFSDAWMDWVRHSPEKGLEWVAELRSKAFNHAT
YYAESVKGRFTISRDDSKSTVYLMNSLRAEDTGIYYCTPNWDEGFAYWGQGTTLTVSA
(SEQ ID NO:23) and a VL comprising the amino acid sequence of

NIMMTQSPSSLVVSAGEKVTMSCKSSHSVLYSSNQKNYLAWYQQKPGQSPKLLIWASTKNS
GVPDRFTGSGSGTDFTLTISVQAEDLAVYYCHQYLSSYTFGGGTKLEIK (SEQ ID NO:24).

307. An anti-glyco-LAMP1 antibody or antigen-binding fragment, which is optionally
an anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 1 to
298, which comprises a VH comprising an amino acid sequence having at least 95% sequence
identity to

EVRLEESGGGLVQPGGSMKLSCVASGFTFSDAWMDWVRQSPERGLEWVAELRSKTFNHAT
YYAESVRGRFTISRDDSKSTVYLMNSLRAEDTGIYYCSPNWDEGFAYWGQGTTLTVSA
(SEQ ID NO:45) and a VL comprising an amino acid sequence having at least 95% sequence
identity to

DVVMTQIPLSLCVSLGDQASISCRSSQSLVHNNNGNTYLHWYLQKPGQSPKLLINKVSKRFTGV
PDRFSGSGSGTDFTLKISRVEAEDLGVYFCSQSTHVPRTFGGGTKLEIK (SEQ ID NO:46).

308. An anti-glyco-LAMP1 antibody or antigen-binding fragment, which is optionally
an anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 1 to 298
or 307, which comprises a VH comprising an amino acid sequence having at least 97%
sequence identity to

EVRLEESGGGLVQPGGSMKLSCVASGFTFSDAWMDWVRQSPERGLEWVAELRSKTFNHAT
YYAESVRGRFTISRDDSKSTVYLMNSLRAEDTGIYYCSPNWDEGFAYWGQGTTLTVSA
(SEQ ID NO:45) and a VL comprising an amino acid sequence having at least 97% sequence
identity to

DVVMTQIPLSLCVSLGDQASISCRSSQSLVHNNNGNTYLHWYLQKPGQSPKLLINKVSKRFTGV
PDRFSGSGSGTDFTLKISRVEAEDLGVYFCSQSTHVPRTFGGGTKLEIK (SEQ ID NO:46).

309. An anti-glyco-LAMP1 antibody or antigen-binding fragment, which is optionally
an anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 1 to
298, 307, or 308, which comprises a VH comprising an amino acid sequence having at least

99% sequence identity to

EVRLEESGGGLVQPGGSMKLSCVASGFTFSDAWMDWVRQSPERGLEWVAELRSKTFNHAT
YYAESVRGRFTISRDDSKSTVYLLQMNSLRAEDTGIYYCSPNWDEGFAYWGQGTLLTVSA
(SEQ ID NO:45) and a VL comprising an amino acid sequence having at least 99% sequence
identity to

DVWMTQIPLSLCVSLGDQASISCRSSQSLVHNNNGNTYLHWYLQKPGQSPKLLINKVSKRFTGV
PDRFSGSGSGTDFTLKISRVEAEDLGVYFCSQSTHVPRTFGGGTKLEIK (SEQ ID NO:46).

310. An anti-glyco-LAMP1 antibody or antigen-binding fragment, which is optionally
an anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 1 to 298
or 307 to 309, which comprises a VH comprising the amino acid sequence of

EVRLEESGGGLVQPGGSMKLSCVASGFTFSDAWMDWVRQSPERGLEWVAELRSKTFNHAT
YYAESVRGRFTISRDDSKSTVYLLQMNSLRAEDTGIYYCSPNWDEGFAYWGQGTLLTVSA
(SEQ ID NO:45) and a VL comprising the amino acid sequence of

DVWMTQIPLSLCVSLGDQASISCRSSQSLVHNNNGNTYLHWYLQKPGQSPKLLINKVSKRFTGV
PDRFSGSGSGTDFTLKISRVEAEDLGVYFCSQSTHVPRTFGGGTKLEIK (SEQ ID NO:46).

311. An anti-glyco-LAMP1 antibody or antigen-binding fragment, which is optionally
anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 1 to 298,
which comprises a VH comprising an amino acid sequence having at least 95% sequence
identity to any one of SEQ ID NOS:133-144 (the "VH reference sequence") and a VL
comprising an amino acid sequence having at least 95% sequence identity to any one of SEQ
ID NOS:145-153 (the "VL reference sequence").

312. The anti-glyco-LAMP1 antibody or antigen-binding fragment of embodiment 311,
which comprises a VH comprising an amino acid sequence having at least 97% sequence
identity to the VH reference sequence and a VL comprising an amino acid sequence having at
least 97% sequence identity to the VL reference sequence.

313. The anti-glyco-LAMP1 antibody or antigen-binding fragment of embodiment 311,
which comprises a VH comprising an amino acid sequence having at least 99% sequence
identity to the VH reference sequence and a VL comprising an amino acid sequence having at
least 97% sequence identity to the VL reference sequence.

314. The anti-glyco-LAMP1 antibody or antigen-binding fragment of embodiment 311,
which comprises a VH comprising an amino acid sequence having 100% sequence identity to
the VH reference sequence and a VL comprising an amino acid sequence having 100%
sequence identity to the VL reference sequence.

315. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of
embodiments 311 to 315, wherein the VH reference sequence is SEQ ID NO:133.

316. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 311 to 315, wherein the VH reference sequence is SEQ ID NO:134.

317. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 311 to 315, wherein the VH reference sequence is SEQ ID NO:135.

318. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 311 to 315, wherein the VH reference sequence is SEQ ID NO:136.

319. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 311 to 315, wherein the VH reference sequence is SEQ ID NO:137.

320. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 311 to 315, wherein the VH reference sequence is SEQ ID NO:138.

321. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 311 to 315, wherein the VH reference sequence is SEQ ID NO:139.

322. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 311 to 315, wherein the VH reference sequence is SEQ ID NO:140.

323. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 311 to 315, wherein the VH reference sequence is SEQ ID NO:141.

324. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 311 to 315, wherein the VH reference sequence is SEQ ID NO:142.

325. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 311 to 315, wherein the VH reference sequence is SEQ ID NO:143.

326. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 311 to 315, wherein the VH reference sequence is SEQ ID NO:144.

327. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 311 to 326, wherein the VL reference sequence is SEQ ID NO:145.

328. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 311 to 326, wherein the VL reference sequence is SEQ ID NO:146.

329. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 311 to 326, wherein the VL reference sequence is SEQ ID NO:147.

330. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 311 to 326, wherein the VL reference sequence is SEQ ID NO:148.

331. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 311 to 326, wherein the VL reference sequence is SEQ ID NO:149.

332. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 311 to 326, wherein the VL reference sequence is SEQ ID NO:150.

333. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 311 to 326, wherein the VL reference sequence is SEQ ID NO:151.

334. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 311 to 326, wherein the VL reference sequence is SEQ ID NO:152.

335. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 311 to 326, wherein the VL reference sequence is SEQ ID NO:153.

336. An anti-glyco-LAMP1 antibody or antigen-binding fragment, which is optionally an anti-glyco-LAMP1 antibody or antigen-binding fragment according to any one of embodiments 1 to 335, that competes with a reference antibody or antigen binding fragment comprising:

- (a) a heavy chain variable (VH) sequence of
 EVKLEESGGGLVQPGGSMKVSCGASGFTFSDAWMDWWRQSPEKGLE
 WWAEMRSKAFNHAIYYAESVKGRFTISRDDSKSRVYLQMNLRLPEDTGI
 YYCTPNWDEGFAYWGQGTTLTVSA (SEQ ID NO:1) and a light chain
 variable (VL) sequence of
 DVMLTQTPLSLPVSLGDQASISCRSSQSLVHSNGNTYLHWYLQKPGQS
 PKLLINKVSNRFFGVPDRFSGSGSGTDFTLKISRVEAEDLGVYFCSQST
 HVPRTFGGGTKLEIK (SEQ ID NO:2);
- (b) a heavy chain variable (VH) sequence of
 EVKLEDSGGGLVQPGGSMKLSCAASGFTFSDAWMDWWRHSPEKGLE
 WWAELRSKAFNHATYYAESVKGRFTISRDDSKSTVYLQMNSLRAEDTG
 IYYCTPNWDEGFAYWGQGTTLTVSA (SEQ ID NO:23) and a light chain
 variable (VL) sequence of
 NIMMTQSPSSLVVSAGEKVTMSCKSSHSVLYSSNQKNYLAWYQQKPG
 QSPKLLIYWASTKNSGVPDRFTGSGSGTDFTLTISVQAEDLAVYYCHQ
 YLSSYTFGGGTKLEIK (SEQ ID NO:24);
- (c) a heavy chain variable (VH) sequence of
 EVRLEESGGGLVQPGGSMKLSCVASGFTFSDAWMDWWRQSPERGLE
 WWAELRSKTFNHATYYAESVRGRFTISRDDSKSTVYLQMNSLRAEDTG
 IYYCSPNWDEGFAYWGQGTTLTVSA (SEQ ID NO:45) and a light chain
 variable (VL) sequence of
 DVVMTQIPLSLCVSLGDQASISCRSSQSLVHNNGNTYLHWYLQKPGQS
 PKLLINKVSKRFTGVPDRFSGSGSGTDFTLKISRVEAEDLGVYFCSQST
 HVPRTFGGGTKLEIK (SEQ ID NO:46); or
- (d) a humanized heavy chain variable (VH) sequence of 13C3 (e.g., any one of SEQ ID NOS:133-144) and a humanized light chain variable (VL) sequence of 13C3 (e.g., any one of SEQ ID NOS:145-153),

for binding to:

- (a) a LAMP1 peptide comprising CEQDRPSP**IT**APPAPPSPSP (SEQ ID NO:200) or a fragment thereof that has been glycosylated with GalNAc on the threonine residue shown with bold and underlined text (“the first LAMP1 glycopeptide”);

- (b) a LAMP1 peptide comprising CEQDRPSP**TT**APPAPPSPSP (SEQ ID NO:216) or a fragment thereof that has been glycosylated with GalNAc on the threonine residues shown with bold and underlined text ("the second LAMP1 glycopeptide");
- (c) a LAMP1 peptide comprising CEQDRP**SP****TT**APPAPPSPSP (SEQ ID NO:217) or a fragment thereof that has been glycosylated with GalNAc on the serine and threonine residues shown with bold and underlined text ("the third LAMP1 glycopeptide"); or
- (d) a LAMP1 peptide comprising CEQDRP**SP****TT**APPAPPSPSP (SEQ ID NO:154) or a fragment thereof that has been glycosylated with GalNAc on the serine and threonine residues shown with bold and underlined text ("the fourth LAMP1 glycopeptide"), the anti-glyco-LAMP1 antibody or antigen-binding fragment comprising:
 - (i) a VH sequence with first, second and third CDR means within the VH sequence; and
 - (ii) a VL sequence with fourth, fifth and sixth CDR means within the VL sequence,

wherein the first, second, third, fourth, fifth, and sixth CDR means cooperate to effect binding of the anti-glyco-LAMP1 antibody or antigen-binding fragment to the first LAMP1 glycopeptide, the second LAMP1 glycopeptide, the third LAMP1 glycopeptide, or the fourth LAMP1 glycopeptide.

337. An anti-glyco-LAMP1 antibody or antigen-binding fragment that competes with a reference antibody or antigen binding fragment comprising:

- (a) a heavy chain variable (VH) sequence of
 EVKLEESGGGLVQPGGSMKVSCGASGFTFSDAWMDWVRQSPEKGLE
 WVAEMRSKAFNHAIYYAESVKGRFTISRDDSKSRVYLQMNLRLPEDTGI
 YYCTPNWDEGFAYWGQGLTVTVSA (SEQ ID NO:1) and a light chain
 variable (VL) sequence of
 DVMLTQTPLSLPVSLGDQASISCRSSQSLVHSNGNTYLHWYLQKPGQSS
 PKLLINKVSNRFFGVPDRFSGSGSGTDFTLKISRVEAEDLGVYFCSQST
 HVPRTFGGGTKLEIK (SEQ ID NO:2);
- (b) a heavy chain variable (VH) sequence of
 EVKLEDGGGLVQPGGSMKLSAASGFTFSDAWMDWVRHSPEKGLE
 WVAELRSKAFNHATYYAESVKGRFTISRDDSKSTVYLQMNSLRAEDTG
 IYYCTPNWDEGFAYWGQGLTVTVSA (SEQ ID NO:23) and a light chain
 variable (VL) sequence of
 NIMMTQSPSSLVVSAGEKVTMSCKSSHSVLYSSNQKNYLAWYQQKPG

QSPKLLIYWASTKNSGVPDRFTGSGSGTDFTLTISSVQAEDLAVYYCHQ
YLSSYTFGGGTKLEIK (SEQ ID NO:24);

- (c) a heavy chain variable (VH) sequence of
EVRLEESGGGLVQPGGSMKLSVASGFTFSDAWMDWVRQSPERGLE
WVAELRSKTFNHATYYAESVRGRFTISRDDSKSTVYLQMNSLRAEDTG
IYYCSPNWDEGFAYWGQGLTVTVSA (SEQ ID NO:45) and a light chain
variable (VL) sequence of
DVVMTQIPLSLCVSLGDQASISCRSSQSLVHNNGNTYLHWYLQKPGQS
PKLLINKVSKRFTGVPDRFSGSGSGTDFTLKISRVEAEDLGVYFCSQST
HVPRTFGGGTKLEIK (SEQ ID NO:46); or
- (d) a humanized heavy chain variable (VH) sequence of 13C3 (e.g., any one
of SEQ ID NOS:133-144) and a humanized light chain variable (VL)
sequence of 13C3 (e.g., any one of SEQ ID NOS:145-153),

for binding to:

- (a) a LAMP1 peptide comprising CEQDRPSP**IT**APPAPPSPSP (SEQ ID
NO:200) or a fragment thereof that has been glycosylated with GalNAc
on the threonine residue shown with bold and underlined text ("the first
LAMP1 glycopeptide");
- (b) a LAMP1 peptide comprising CEQDRPSP**TT**APPAPPSPSP (SEQ ID
NO:216) or a fragment thereof that has been glycosylated with GalNAc
on the threonine residues shown with bold and underlined text ("the
second LAMP1 glycopeptide");
- (c) a LAMP1 peptide comprising CEQDRP**SP****IT**APPAPPSPSP (SEQ ID
NO:217) or a fragment thereof that has been glycosylated with GalNAc
on the serine and threonine residues shown with bold and underlined text
("the third LAMP1 glycopeptide"); or
- (d) a LAMP1 peptide comprising CEQDRP**SP****TT**APPAPPSPSP (SEQ ID
NO:154) or a fragment thereof that has been glycosylated with GalNAc
on the serine and threonine residues shown with bold and underlined text
("the fourth LAMP1 glycopeptide"),

the anti-glyco-LAMP1 antibody or antigen-binding fragment comprising a means
for binding the LAMP1 glycopeptide.

338. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 337,
wherein the means for binding the LAMP1 glycopeptide comprises a heavy chain variable (VH)
domain and a light chain variable (VL) domain.

339. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of
embodiments 336 to 338 that competes with the reference antibody or antigen binding fragment
for binding to the first LAMP1 glycopeptide.

340. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of embodiments 336 to 338 that competes with the reference antibody or antigen binding fragment for binding to the second LAMP1 glycopeptide.

341. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of embodiments 336 to 338 that competes with the reference antibody or antigen binding fragment for binding to the third LAMP1 glycopeptide.

342. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of embodiments 336 to 338 that competes with the reference antibody or antigen binding fragment for binding to the fourth LAMP1 glycopeptide.

343. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of embodiments 336 to 342, wherein the fragment of the first LAMP1 glycopeptide, the second LAMP1 glycopeptide, the third LAMP1 glycopeptide, or the fourth LAMP1 glycopeptide comprises amino acids 5-11, 5-12, 5-13, 5-14, 5-15, 5-16, 5-17, 5-18, 5-19, or 5-20 of SEQ ID NO:200, 216, 217, or 154, respectively.

344. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of embodiments 336 to 342, wherein the fragment of the first LAMP1 glycopeptide, the second LAMP1 glycopeptide, the third LAMP1 glycopeptide, or the fourth LAMP1 glycopeptide comprises amino acids 4-11, 4-12, 4-13, 4-14, 4-15, 4-16, 4-17, 4-18, 4-19, or 4-20 of SEQ ID NO:200, 216, 217, or 154, respectively.

345. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of embodiments 336 to 342, wherein the fragment of the first LAMP1 glycopeptide, the second LAMP1 glycopeptide, the third LAMP1 glycopeptide, or the fourth LAMP1 glycopeptide comprises amino acids 3-11, 3-12, 3-13, 3-14, 3-15, 3-16, 3-17, 3-18, 3-19, or 3-20 of SEQ ID NO:200, 216, 217, or 154, respectively.

346. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of embodiments 336 to 342, wherein the fragment of the first LAMP1 glycopeptide, the second LAMP1 glycopeptide, the third LAMP1 glycopeptide, or the fourth LAMP1 glycopeptide comprises amino acids 2-11, 2-12, 2-13, 2-14, 2-15, 2-16, 2-17, 2-18, 2-19, or 2-20 of SEQ ID NO:200, 216, 217, or 154, respectively.

347. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of embodiments 336 to 342, wherein the fragment of the first LAMP1 glycopeptide, the second LAMP1 glycopeptide, the third LAMP1 glycopeptide, or the fourth LAMP1 glycopeptide comprises amino acids 1-11, 1-12, 1-13, 1-14, 1-15, 1-16, 1-17, 1-18, 1-19, or 1-20 of SEQ ID NO:200, 216, 217, or 154, respectively.

348. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 336 to 347 wherein the anti-glyco-LAMP1 antibody or antigen-binding fragment competes with a reference antibody or antigen binding fragment comprising a VH sequence of EVKLEESGGGLVQPGGSMKVSCGASGFTFSDAWMDWVRQSPEKGLEWVAEMRSKAFNHAI

YYAESVKGRFTISRDDSKSRVYLQMNLLRPEDTGIYYCTPNWDEGFAYWGQGTTLVTVSA (SEQ ID NO:1) and a VL sequence of DVMLTQTPLSLPVSLGDQASISCRSSQSLVHSNGNTYLHWYLQKPGQSPKLLINKVSNRFFGV PDRFSGSGSGTDFTLKISRVEAEDLGVYFCSQSTHVPRTFGGGTKLEIK (SEQ ID NO:2).

349. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 336 to 347 wherein the anti-glyco-LAMP1 antibody or antigen-binding fragment competes with a reference antibody or antigen binding fragment comprising a VH sequence of EVKLEDSGGGLVQPGGSMKLSCAASGFTFSDAWMDWVRHSPEKGLEWVAELRSKAFNHAT YYAESVKGRFTISRDDSKSTVYLQMNSLRAEDTGIYYCTPNWDEGFAYWGQGTTLVTVSA (SEQ ID NO:23) and a VL sequence of EVKLEDSGGGLVQPGGSMKLSCAASGFTFSDAWMDWVRHSPEKGLEWVAELRSKAFNHAT YYAESVKGRFTISRDDSKSTVYLQMNSLRAEDTGIYYCTPNWDEGFAYWGQGTTLVTVSA (SEQ ID NO:23).

350. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 336 to 347 wherein the anti-glyco-LAMP1 antibody or antigen-binding fragment competes with a reference antibody or antigen binding fragment comprising a VH sequence of EVRLEESGGGLVQPGGSMKLSCVASGFTFSDAWMDWVRQSPERGLEWVAELRSKTFNHAT YYAESVRGRFTISRDDSKSTVYLQMNSLRAEDTGIYYCSPNWDEGFAYWGQGTTLVTVSA (SEQ ID NO:45) and a VL sequence of DVVMTQIPLSLCVSLGDQASISCRSSQSLVHNNGNTYLHWYLQKPGQSPKLLINKVSKRFTGV PDRFSGSGSGTDFTLKISRVEAEDLGVYFCSQSTHVPRTFGGGTKLEIK (SEQ ID NO:46).

351. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 336 to 347 wherein the anti-glyco-LAMP1 antibody or antigen-binding fragment competes with a reference antibody or antigen binding fragment comprising a humanized heavy chain variable (VH) sequence of 13C3 (e.g., any one of SEQ ID NOS:133-144) and a humanized light chain variable (VL) sequence of 13C3 (e.g., any one of SEQ ID NOS:145-153).

352. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 1 to 351, which preferentially binds to a glyco-LAMP1 epitope that is overexpressed on cancer cells as compared to normal cells.

353. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 1 to 352, which specifically binds to the first LAMP1 glycopeptide.

354. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 1 to 353, which specifically binds to the second LAMP1 glycopeptide.

355. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 1 to 354, which specifically binds to the third LAMP1 glycopeptide.

356. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 1 to 355, which specifically binds to the fourth LAMP1 glycopeptide.

357. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 1 to 352, which does not specifically bind to the first LAMP1 glycopeptide.

358. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 1 to 352 or 357, which does not specifically bind to the second LAMP1 glycopeptide.

359. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 1 to 352, 357, or 358, which does not specifically bind to the third LAMP1 glycopeptide.

360. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 1 to 352 or 357 to 359, which does not specifically bind to the fourth LAMP1 glycopeptide.

361. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 360, which binds to the first LAMP1 glycopeptide with a binding affinity (KD) of 1 nM to 200 nM as measured by surface plasmon resonance or bio-layer interferometry.

362. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 360, which binds to the first LAMP1 glycopeptide with a binding affinity (KD) of 1 nM to 150 nM as measured by surface plasmon resonance or bio-layer interferometry.

363. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 360, which binds to the first glycopeptide with a binding affinity (KD) of 1 nM to 100 nM as measured by surface plasmon resonance or bio-layer interferometry.

364. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 360, which binds to the first LAMP1 glycopeptide with a binding affinity (KD) of 1 nM to 50 nM as measured by surface plasmon resonance or bio-layer interferometry.

365. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 360, which binds to the first LAMP1 glycopeptide with a binding affinity (KD) of 5 nM to 200 nM as measured by surface plasmon resonance or bio-layer interferometry.

366. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 360, which binds to the first LAMP1 glycopeptide with a binding affinity (KD) of 5 nM to 100 nM as measured by surface plasmon resonance or bio-layer interferometry.

367. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 360, which binds to the first LAMP1 glycopeptide with a binding affinity (KD) of 5 nM to 50 nM as measured by surface plasmon resonance or bio-layer interferometry.

368. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 360, which binds to the first LAMP1 glycopeptide with a binding affinity (KD) of 5 nM to 25 nM as measured by surface plasmon resonance or bio-layer interferometry.

369. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 360, which binds to the first LAMP1 glycopeptide with a binding affinity (KD) of 5 nM to 10 nM as measured by surface plasmon resonance or bio-layer interferometry.

370. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 360, which binds to the first LAMP1 glycopeptide with a binding affinity (KD) of 10 nM to 200 nM as measured by surface plasmon resonance or bio-layer interferometry.

371. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 360, which binds to the first LAMP1 glycopeptide with a binding affinity (KD) of 10 nM to 100 nM as measured by surface plasmon resonance or bio-layer interferometry.

372. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 360, which binds to the first LAMP1 glycopeptide with a binding affinity (KD) of 10 nM to 150 nM as measured by surface plasmon resonance or bio-layer interferometry.

373. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 360, which binds to the first LAMP1 glycopeptide with a binding affinity (KD) of 10 nM to 100 nM as measured by surface plasmon resonance or bio-layer interferometry.

374. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 360, which binds to the first LAMP1 glycopeptide with a binding affinity (KD) of 10 nM to 50 nM as measured by surface plasmon resonance or bio-layer interferometry.

375. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 360, which binds to the first LAMP1 glycopeptide with a binding affinity (KD) of 10 nM to 25 nM as measured by surface plasmon resonance or bio-layer interferometry.

376. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 360, which binds to the first LAMP1 glycopeptide with a binding affinity (KD) of 50 nM to 200 nM as measured by surface plasmon resonance or bio-layer interferometry.

377. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 360, which binds to the first LAMP1 glycopeptide with a binding affinity (KD) of 50 nM to 150 nM as measured by surface plasmon resonance or bio-layer interferometry.

378. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 360, which binds to the first LAMP1 glycopeptide with a binding affinity (KD) of 50 nM to 100 nM as measured by surface plasmon resonance or bio-layer interferometry.

379. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 360, which binds to the first LAMP1 glycopeptide with a binding affinity (KD) of 100 nM to 200 nM as measured by surface plasmon resonance or bio-layer interferometry.

380. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 360, which binds to the first LAMP1 glycopeptide with a binding affinity (KD) of 100 nM to 150 nM as measured by surface plasmon resonance or bio-layer interferometry.

381. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 360, which binds to the second LAMP1 glycopeptide with a binding affinity (KD) of 1 nM to 200 nM as measured by surface plasmon resonance or bio-layer interferometry.

382. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 360, which binds to the second LAMP1 glycopeptide with a binding affinity (KD) of 1 nM to 150 nM as measured by surface plasmon resonance or bio-layer interferometry.

383. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 360, which binds to the second glycopeptide with a binding affinity (KD) of 1 nM to 100 nM as measured by surface plasmon resonance or bio-layer interferometry.

384. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 360, which binds to the second LAMP1 glycopeptide with a binding affinity (KD) of 1 nM to 50 nM as measured by surface plasmon resonance or bio-layer interferometry.

385. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 360, which binds to the second LAMP1 glycopeptide with a binding affinity (KD) of 5 nM to 200 nM as measured by surface plasmon resonance or bio-layer interferometry.

386. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 360, which binds to the second LAMP1 glycopeptide with a binding affinity (KD) of 5 nM to 100 nM as measured by surface plasmon resonance or bio-layer interferometry.

387. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 360, which binds to the second LAMP1 glycopeptide with a binding affinity (KD) of 5 nM to 50 nM as measured by surface plasmon resonance or bio-layer interferometry.

388. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 360, which binds to the second LAMP1 glycopeptide with a binding affinity (KD) of 5 nM to 25 nM as measured by surface plasmon resonance or bio-layer interferometry.

389. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 360, which binds to the second LAMP1 glycopeptide with a binding affinity (KD) of 5 nM to 10 nM as measured by surface plasmon resonance or bio-layer interferometry.

390. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 360, which binds to the second LAMP1 glycopeptide with a binding affinity (KD) of 10 nM to 200 nM as measured by surface plasmon resonance or bio-layer interferometry.

391. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 360, which binds to the second LAMP1 glycopeptide with a binding affinity (KD) of 10 nM to 100 nM as measured by surface plasmon resonance or bio-layer interferometry.

392. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 360, which binds to the second LAMP1 glycopeptide with a binding affinity

(KD) of 10 nM to 150 nM as measured by surface plasmon resonance or bio-layer interferometry.

393. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 360, which binds to the second LAMP1 glycopeptide with a binding affinity (KD) of 10 nM to 100 nM as measured by surface plasmon resonance or bio-layer interferometry.

394. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 360, which binds to the second LAMP1 glycopeptide with a binding affinity (KD) of 10 nM to 50 nM as measured by surface plasmon resonance or bio-layer interferometry.

395. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 360, which binds to the second LAMP1 glycopeptide with a binding affinity (KD) of 10 nM to 25 nM as measured by surface plasmon resonance or bio-layer interferometry.

396. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 360, which binds to the second LAMP1 glycopeptide with a binding affinity (KD) of 50 nM to 200 nM as measured by surface plasmon resonance or bio-layer interferometry.

397. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 360, which binds to the second LAMP1 glycopeptide with a binding affinity (KD) of 50 nM to 150 nM as measured by surface plasmon resonance or bio-layer interferometry.

398. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 360, which binds to the second LAMP1 glycopeptide with a binding affinity (KD) of 50 nM to 100 nM as measured by surface plasmon resonance or bio-layer interferometry.

399. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 360, which binds to the second LAMP1 glycopeptide with a binding affinity (KD) of 100 nM to 200 nM as measured by surface plasmon resonance or bio-layer interferometry.

400. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 360, which binds to the second LAMP1 glycopeptide with a binding affinity (KD) of 100 nM to 150 nM as measured by surface plasmon resonance or bio-layer interferometry.

401. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 360, which binds to the third LAMP1 glycopeptide with a binding affinity (KD) of 1 nM to 200 nM as measured by surface plasmon resonance or bio-layer interferometry.

402. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 360, which binds to the third LAMP1 glycopeptide with a binding affinity (KD) of 1 nM to 150 nM as measured by surface plasmon resonance or bio-layer interferometry.

403. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 360, which binds to the third glycopeptide with a binding affinity (KD) of 1 nM to 100 nM as measured by surface plasmon resonance or bio-layer interferometry.

404. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 360, which binds to the third LAMP1 glycopeptide with a binding affinity (KD) of 1 nM to 50 nM as measured by surface plasmon resonance or bio-layer interferometry.

405. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 360, which binds to the third LAMP1 glycopeptide with a binding affinity (KD) of 5 nM to 200 nM as measured by surface plasmon resonance or bio-layer interferometry.

406. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 360, which binds to the third LAMP1 glycopeptide with a binding affinity (KD) of 5 nM to 100 nM as measured by surface plasmon resonance or bio-layer interferometry.

407. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 360, which binds to the third LAMP1 glycopeptide with a binding affinity (KD) of 5 nM to 50 nM as measured by surface plasmon resonance or bio-layer interferometry.

408. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 360, which binds to the third LAMP1 glycopeptide with a binding affinity (KD) of 5 nM to 25 nM as measured by surface plasmon resonance or bio-layer interferometry.

409. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 360, which binds to the third LAMP1 glycopeptide with a binding affinity (KD) of 5 nM to 10 nM as measured by surface plasmon resonance or bio-layer interferometry.

410. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 360, which binds to the third LAMP1 glycopeptide with a binding affinity (KD) of 10 nM to 200 nM as measured by surface plasmon resonance or bio-layer interferometry.

411. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 360, which binds to the third LAMP1 glycopeptide with a binding affinity (KD) of 10 nM to 100 nM as measured by surface plasmon resonance or bio-layer interferometry.

412. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 360, which binds to the third LAMP1 glycopeptide with a binding affinity (KD) of 10 nM to 150 nM as measured by surface plasmon resonance or bio-layer interferometry.

413. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 360, which binds to the third LAMP1 glycopeptide with a binding affinity (KD) of 10 nM to 100 nM as measured by surface plasmon resonance or bio-layer interferometry.

414. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 360, which binds to the third LAMP1 glycopeptide with a binding affinity (KD) of 10 nM to 50 nM as measured by surface plasmon resonance or bio-layer interferometry.

415. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 360, which binds to the third LAMP1 glycopeptide with a binding affinity (KD) of 10 nM to 25 nM as measured by surface plasmon resonance or bio-layer interferometry.

416. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 360, which binds to the third LAMP1 glycopeptide with a binding affinity (KD) of 50 nM to 200 nM as measured by surface plasmon resonance or bio-layer interferometry.

417. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 360, which binds to the third LAMP1 glycopeptide with a binding affinity (KD) of 50 nM to 150 nM as measured by surface plasmon resonance or bio-layer interferometry.

418. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 360, which binds to the third LAMP1 glycopeptide with a binding affinity (KD) of 50 nM to 100 nM as measured by surface plasmon resonance or bio-layer interferometry.

419. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 360, which binds to the third LAMP1 glycopeptide with a binding affinity (KD) of 100 nM to 200 nM as measured by surface plasmon resonance or bio-layer interferometry.

420. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 360, which binds to the third LAMP1 glycopeptide with a binding affinity (KD) of 100 nM to 150 nM as measured by surface plasmon resonance or bio-layer interferometry.

421. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 360, which binds to the fourth LAMP1 glycopeptide with a binding affinity (KD) of 1 nM to 200 nM as measured by surface plasmon resonance or bio-layer interferometry.

422. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 360, which binds to the fourth LAMP1 glycopeptide with a binding affinity (KD) of 1 nM to 150 nM as measured by surface plasmon resonance or bio-layer interferometry.

423. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 360, which binds to the fourth glycopeptide with a binding affinity (KD) of 1 nM to 100 nM as measured by surface plasmon resonance or bio-layer interferometry.

424. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 360, which binds to the fourth LAMP1 glycopeptide with a binding affinity (KD) of 1 nM to 50 nM as measured by surface plasmon resonance or bio-layer interferometry.

425. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 360, which binds to the fourth LAMP1 glycopeptide with a binding affinity

(KD) of 5 nM to 200 nM as measured by surface plasmon resonance or bio-layer interferometry.

426. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 360, which binds to the fourth LAMP1 glycopeptide with a binding affinity (KD) of 5 nM to 100 nM as measured by surface plasmon resonance or bio-layer interferometry.

427. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 360, which binds to the fourth LAMP1 glycopeptide with a binding affinity (KD) of 5 nM to 50 nM as measured by surface plasmon resonance or bio-layer interferometry.

428. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 360, which binds to the fourth LAMP1 glycopeptide with a binding affinity (KD) of 5 nM to 25 nM as measured by surface plasmon resonance or bio-layer interferometry.

429. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 360, which binds to the fourth LAMP1 glycopeptide with a binding affinity (KD) of 5 nM to 10 nM as measured by surface plasmon resonance or bio-layer interferometry.

430. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 360, which binds to the fourth LAMP1 glycopeptide with a binding affinity (KD) of 10 nM to 200 nM as measured by surface plasmon resonance or bio-layer interferometry.

431. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 360, which binds to the fourth LAMP1 glycopeptide with a binding affinity (KD) of 10 nM to 100 nM as measured by surface plasmon resonance or bio-layer interferometry.

432. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 360, which binds to the fourth LAMP1 glycopeptide with a binding affinity (KD) of 10 nM to 150 nM as measured by surface plasmon resonance or bio-layer interferometry.

433. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 360, which binds to the fourth LAMP1 glycopeptide with a binding affinity (KD) of 10 nM to 100 nM as measured by surface plasmon resonance or bio-layer interferometry.

434. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 360, which binds to the fourth LAMP1 glycopeptide with a binding affinity (KD) of 10 nM to 50 nM as measured by surface plasmon resonance or bio-layer interferometry.

435. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 360, which binds to the fourth LAMP1 glycopeptide with a binding affinity

(KD) of 10 nM to 25 nM as measured by surface plasmon resonance or bio-layer interferometry.

436. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 360, which binds to the fourth LAMP1 glycopeptide with a binding affinity (KD) of 50 nM to 200 nM as measured by surface plasmon resonance or bio-layer interferometry.

437. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 360, which binds to the fourth LAMP1 glycopeptide with a binding affinity (KD) of 50 nM to 150 nM as measured by surface plasmon resonance or bio-layer interferometry.

438. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 360, which binds to the fourth LAMP1 glycopeptide with a binding affinity (KD) of 50 nM to 100 nM as measured by surface plasmon resonance or bio-layer interferometry.

439. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 360, which binds to the fourth LAMP1 glycopeptide with a binding affinity (KD) of 100 nM to 200 nM as measured by surface plasmon resonance or bio-layer interferometry.

440. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 360, which binds to the fourth LAMP1 glycopeptide with a binding affinity (KD) of 100 nM to 150 nM as measured by surface plasmon resonance or bio-layer interferometry.

441. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 440, in which the binding affinity to the first LAMP1 glycopeptide, second LAMP1 glycopeptide, third LAMP1 glycopeptide, or fourth LAMP1 glycopeptide is as measured by surface plasmon resonance.

442. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 440, in which the binding affinity to the first LAMP1 glycopeptide, second LAMP1 glycopeptide, third LAMP1 glycopeptide, or fourth LAMP1 glycopeptide is as measured by bio-layer interferometry.

443. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 442, which does not specifically bind to the unglycosylated LAMP1 peptide CEQDRPSPTTAPPAPPSPSP (SEQ ID NO: 155) (the “unglycosylated LAMP1 peptide”).

444. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 443, which has a binding affinity to the LAMP1 glycopeptide which is at least 3 times the binding affinity of the anti-glyco-LAMP1 antibody or antigen-binding fragment to the unglycosylated LAMP1 peptide, optionally wherein the binding affinity is measured by surface plasmon resonance, and further optionally where in the surface plasmon resonance is

measured in the presence of saturating amounts of either the LAMP1 glycopeptide or the unglycosylated LAMP1 peptide (e.g., about 1 μ M, about 1.5 μ M, or about 2 μ M of either peptide).

445. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 444, which has a binding affinity to the LAMP1 glycopeptide which is at least 5 times the binding affinity of the anti-glyco-LAMP1 antibody or antigen-binding fragment to the unglycosylated LAMP1 peptide, optionally wherein the binding affinity is measured by surface plasmon resonance, and further optionally where in the surface plasmon resonance is measured in the presence of saturating amounts of either the LAMP1 glycopeptide or the unglycosylated LAMP1 peptide (e.g., about 1 μ M, about 1.5 μ M, or about 2 μ M of either peptide).

446. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 445, which has a binding affinity to the LAMP1 glycopeptide which is at least 10 times the binding affinity of the anti-glyco-LAMP1 antibody or antigen-binding fragment to the unglycosylated LAMP1 peptide, optionally wherein the binding affinity is measured by surface plasmon resonance, and further optionally where in the surface plasmon resonance is measured in the presence of saturating amounts of either the LAMP1 glycopeptide or the unglycosylated LAMP1 peptide (e.g., about 1 μ M, about 1.5 μ M, or about 2 μ M of either peptide).

447. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 446, which has a binding affinity to the LAMP1 glycopeptide which is at least 20 times the binding affinity of the anti-glyco-LAMP1 antibody or antigen-binding fragment to the unglycosylated LAMP1 peptide, optionally wherein the binding affinity is measured by surface plasmon resonance, and further optionally where in the surface plasmon resonance is measured in the presence of saturating amounts of either the LAMP1 glycopeptide or the unglycosylated LAMP1 peptide (e.g., about 1 μ M, about 1.5 μ M, or about 2 μ M of either peptide).

448. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 447, which has a binding affinity to the LAMP1 glycopeptide which is at least 50 times the binding affinity of the anti-glyco-LAMP1 antibody or antigen-binding fragment to the unglycosylated LAMP1 peptide, optionally wherein the binding affinity is measured by surface plasmon resonance, and further optionally where in the surface plasmon resonance is measured in the presence of saturating amounts of either the LAMP1 glycopeptide or the unglycosylated LAMP1 peptide (e.g., about 1 μ M, about 1.5 μ M, or about 2 μ M of either peptide).

449. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 448, which has a binding affinity to the LAMP1 glycopeptide which is at least 100 times the binding affinity of the anti-glyco-LAMP1 antibody or antigen-binding fragment to

the unglycosylated LAMP1 peptide, optionally wherein the binding affinity is measured by surface plasmon resonance, and further optionally where in the surface plasmon resonance is measured in the presence of saturating amounts of either the LAMP1 glycopeptide or the unglycosylated LAMP1 peptide (e.g., about 1 μ M, about 1.5 μ M, or about 2 μ M of either peptide).

450. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 449, which does not specifically bind to the MUC1 tandem repeat (VTSAPDTRPAPGSTAPPAHG)₃ (SEQ ID NO:208) that has been glycosylated in vitro using purified recombinant human glycosyltransferases GalNAc-T1, GalNAc-T2, and GalNAc-T4 ("the first MUC1 glycopeptide").

451. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 450, which has a binding affinity to the LAMP1 glycopeptide which is at least 3 times the binding affinity of the anti-glyco-LAMP1 antibody or antigen-binding fragment to the first MUC1 glycopeptide, optionally wherein the binding affinity is measured by surface plasmon resonance, and further optionally where in the surface plasmon resonance is measured in the presence of saturating amounts of either the LAMP1 glycopeptide or the first MUC1 peptide (e.g., about 1 μ M, about 1.5 μ M, or about 2 μ M of either peptide).

452. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 451, which has a binding affinity to the LAMP1 glycopeptide which is at least 5 times the binding affinity of the anti-glyco-LAMP1 antibody or antigen-binding fragment to the first MUC1 glycopeptide, optionally wherein the binding affinity is measured by surface plasmon resonance, and further optionally where in the surface plasmon resonance is measured in the presence of saturating amounts of either the LAMP1 glycopeptide or the first MUC1 peptide (e.g., about 1 μ M, about 1.5 μ M, or about 2 μ M of either peptide).

453. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 452, which has a binding affinity to the LAMP1 glycopeptide which is at least 10 times the binding affinity of the anti-glyco-LAMP1 antibody or antigen-binding fragment to the first MUC1 glycopeptide, optionally wherein the binding affinity is measured by surface plasmon resonance, and further optionally where in the surface plasmon resonance is measured in the presence of saturating amounts of either the LAMP1 glycopeptide or the first MUC1 peptide (e.g., about 1 μ M, about 1.5 μ M, or about 2 μ M of either peptide).

454. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 453, which has a binding affinity to the LAMP1 glycopeptide which is at least 20 times the binding affinity of the anti-glyco-LAMP1 antibody or antigen-binding fragment to the first MUC1 glycopeptide, optionally wherein the binding affinity is measured by surface plasmon resonance, and further optionally where in the surface plasmon resonance is measured in the presence of saturating amounts of either the LAMP1 glycopeptide or the first MUC1 peptide (e.g., about 1 μ M, about 1.5 μ M, or about 2 μ M of either peptide).

455. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 454, which has a binding affinity to the LAMP1 glycopeptide which is at least 50 times the binding affinity of the anti-glyco-LAMP1 antibody or antigen-binding fragment to the first MUC1 glycopeptide, optionally wherein the binding affinity is measured by surface plasmon resonance, and further optionally where in the surface plasmon resonance is measured in the presence of saturating amounts of either the LAMP1 glycopeptide or the first MUC1 peptide (e.g., about 1 μ M, about 1.5 μ M, or about 2 μ M of either peptide).

456. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 455, which has a binding affinity to the LAMP1 glycopeptide which is at least 100 times the binding affinity of the anti-glyco-LAMP1 antibody or antigen-binding fragment to the first MUC1 glycopeptide, optionally wherein the binding affinity is measured by surface plasmon resonance, and further optionally where in the surface plasmon resonance is measured in the presence of saturating amounts of either the LAMP1 glycopeptide or the first MUC1 peptide (e.g., about 1 μ M, about 1.5 μ M, or about 2 μ M of either peptide).

457. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 456, which does not specifically bind to the MUC1 peptide TAPPAHGV**TS**APD**TR**PAPG**ST**APPAHGV**T** (SEQ ID NO:209) that has been glycosylated in vitro with GalNAc on the serine and threonine residues shown with bold and underlined text (the "second MUC1 glycopeptide").

458. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 457, which has a binding affinity to the LAMP1 glycopeptide which is at least 3 times the binding affinity of the anti-glyco-LAMP1 antibody or antigen-binding fragment to the second MUC1 glycopeptide, optionally wherein the binding affinity is measured by surface plasmon resonance, and further optionally where in the surface plasmon resonance is measured in the presence of saturating amounts of either the LAMP1 glycopeptide or the second MUC1 peptide (e.g., about 1 μ M, about 1.5 μ M, or about 2 μ M of either peptide).

459. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 458, which has a binding affinity to the LAMP1 glycopeptide which is at least 5 times the binding affinity of the anti-glyco-LAMP1 antibody or antigen-binding fragment to the second MUC1 glycopeptide, optionally wherein the binding affinity is measured by surface plasmon resonance, and further optionally where in the surface plasmon resonance is measured in the presence of saturating amounts of either the LAMP1 glycopeptide or the second MUC1 peptide (e.g., about 1 μ M, about 1.5 μ M, or about 2 μ M of either peptide).

460. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 459, which has a binding affinity to the LAMP1 glycopeptide which is at least 10 times the binding affinity of the anti-glyco-LAMP1 antibody or antigen-binding fragment to the second MUC1 glycopeptide, optionally wherein the binding affinity is measured by surface plasmon resonance, and further optionally where in the surface plasmon resonance is

measured in the presence of saturating amounts of either the LAMP1 glycopeptide or the second MUC1 peptide (e.g., about 1 μ M, about 1.5 μ M, or about 2 μ M of either peptide).

461. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 460, which has a binding affinity to the LAMP1 glycopeptide which is at least 20 times the binding affinity of the anti-glyco-LAMP1 antibody or antigen-binding fragment to the second MUC1 glycopeptide, optionally wherein the binding affinity is measured by surface plasmon resonance, and further optionally where in the surface plasmon resonance is measured in the presence of saturating amounts of either the LAMP1 glycopeptide or the second MUC1 peptide (e.g., about 1 μ M, about 1.5 μ M, or about 2 μ M of either peptide).

462. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 461, which has a binding affinity to the LAMP1 glycopeptide which is at least 50 times the binding affinity of the anti-glyco-LAMP1 antibody or antigen-binding fragment to the second MUC1 glycopeptide, optionally wherein the binding affinity is measured by surface plasmon resonance, and further optionally where in the surface plasmon resonance is measured in the presence of saturating amounts of either the LAMP1 glycopeptide or the second MUC1 peptide (e.g., about 1 μ M, about 1.5 μ M, or about 2 μ M of either peptide).

463. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 462, which has a binding affinity to the LAMP1 glycopeptide which is at least 100 times the binding affinity of the anti-glyco-LAMP1 antibody or antigen-binding fragment to the second MUC1 glycopeptide, optionally wherein the binding affinity is measured by surface plasmon resonance, and further optionally where in the surface plasmon resonance is measured in the presence of saturating amounts of either the LAMP1 glycopeptide or the second MUC1 peptide (e.g., about 1 μ M, about 1.5 μ M, or about 2 μ M of either peptide).

464. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 463, which does not specifically bind to the podoplanin peptide ERG**T**KPPLEELSGK (SEQ ID NO:211) that has been glycosylated in vitro with GalNAc on the threonine residue shown with bold and underlined text (the "PDPN glycopeptide").

465. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 464, which has a binding affinity to the LAMP1 glycopeptide which is at least 3 times the binding affinity of the anti-glyco-LAMP1 antibody or antigen-binding fragment to the PDPN glycopeptide, optionally wherein the binding affinity is measured by surface plasmon resonance, and further optionally where in the surface plasmon resonance is measured in the presence of saturating amounts of either the LAMP1 glycopeptide or the PDPN glycopeptide (e.g., about 1 μ M, about 1.5 μ M, or about 2 μ M of either peptide).

466. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 465, which has a binding affinity to the LAMP1 glycopeptide which is at least 5 times the binding affinity of the anti-glyco-LAMP1 antibody or antigen-binding fragment to the PDPN glycopeptide, optionally wherein the binding affinity is measured by surface plasmon

resonance, and further optionally where in the surface plasmon resonance is measured in the presence of saturating amounts of either the LAMP1 glycopeptide or the PDPN glycopeptide (e.g., about 1 μ M, about 1.5 μ M, or about 2 μ M of either peptide).

467. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 466, which has a binding affinity to the LAMP1 glycopeptide which is at least 10 times the binding affinity of the anti-glyco-LAMP1 antibody or antigen-binding fragment to the PDPN glycopeptide, optionally wherein the binding affinity is measured by surface plasmon resonance, and further optionally where in the surface plasmon resonance is measured in the presence of saturating amounts of either the LAMP1 glycopeptide or the PDPN glycopeptide (e.g., about 1 μ M, about 1.5 μ M, or about 2 μ M of either peptide).

468. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 467, which has a binding affinity to the LAMP1 glycopeptide which is at least 20 times the binding affinity of the anti-glyco-LAMP1 antibody or antigen-binding fragment to the PDPN glycopeptide, optionally wherein the binding affinity is measured by surface plasmon resonance, and further optionally where in the surface plasmon resonance is measured in the presence of saturating amounts of either the LAMP1 glycopeptide or the PDPN glycopeptide (e.g., about 1 μ M, about 1.5 μ M, or about 2 μ M of either peptide).

469. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 468, which has a binding affinity to the LAMP1 glycopeptide which is at least 50 times the binding affinity of the anti-glyco-LAMP1 antibody or antigen-binding fragment to the PDPN glycopeptide, optionally wherein the binding affinity is measured by surface plasmon resonance, and further optionally where in the surface plasmon resonance is measured in the presence of saturating amounts of either the LAMP1 glycopeptide or the PDPN glycopeptide (e.g., about 1 μ M, about 1.5 μ M, or about 2 μ M of either peptide).

470. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 469, which has a binding affinity to the LAMP1 glycopeptide which is at least 100 times the binding affinity of the anti-glyco-LAMP1 antibody or antigen-binding fragment to the PDPN glycopeptide, optionally wherein the binding affinity is measured by surface plasmon resonance, and further optionally where in the surface plasmon resonance is measured in the presence of saturating amounts of either the LAMP1 glycopeptide or the PDPN glycopeptide (e.g., about 1 μ M, about 1.5 μ M, or about 2 μ M of either peptide).

471. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 470, which does not specifically bind to the CD44v6 peptide GYRQ**I**PKEDSH**S**TTGTAAA (SEQ ID NO:212) that has been glycosylated in vitro with GalNAc on the threonine and serine residues shown with bold and underlined text (the “CD44v6 glycopeptide”).

472. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 471, which has a binding affinity to the LAMP1 glycopeptide which is at least

3 times the binding affinity of the anti-glyco-LAMP1 antibody or antigen-binding fragment to the CD44v6 glycopeptide, optionally wherein the binding affinity is measured by surface plasmon resonance, and further optionally where in the surface plasmon resonance is measured in the presence of saturating amounts of either the LAMP1 glycopeptide or the CD44v6 glycopeptide (e.g., about 1 μ M, about 1.5 μ M, or about 2 μ M of either peptide).

473. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 472, which has a binding affinity to the LAMP1 glycopeptide which is at least 5 times the binding affinity of the anti-glyco-LAMP1 antibody or antigen-binding fragment to the CD44v6 glycopeptide, optionally wherein the binding affinity is measured by surface plasmon resonance, and further optionally where in the surface plasmon resonance is measured in the presence of saturating amounts of either the LAMP1 glycopeptide or the CD44v6 glycopeptide (e.g., about 1 μ M, about 1.5 μ M, or about 2 μ M of either peptide).

474. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 473, which has a binding affinity to the LAMP1 glycopeptide which is at least 10 times the binding affinity of the anti-glyco-LAMP1 antibody or antigen-binding fragment to the CD44v6 glycopeptide, optionally wherein the binding affinity is measured by surface plasmon resonance, and further optionally where in the surface plasmon resonance is measured in the presence of saturating amounts of either the LAMP1 glycopeptide or the CD44v6 glycopeptide (e.g., about 1 μ M, about 1.5 μ M, or about 2 μ M of either peptide).

475. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 474, which has a binding affinity to the LAMP1 glycopeptide which is at least 20 times the binding affinity of the anti-glyco-LAMP1 antibody or antigen-binding fragment to the CD44v6 glycopeptide, optionally wherein the binding affinity is measured by surface plasmon resonance, and further optionally where in the surface plasmon resonance is measured in the presence of saturating amounts of either the LAMP1 glycopeptide or the CD44v6 glycopeptide (e.g., about 1 μ M, about 1.5 μ M, or about 2 μ M of either peptide).

476. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 475, which has a binding affinity to the LAMP1 glycopeptide which is at least 50 times the binding affinity of the anti-glyco-LAMP1 antibody or antigen-binding fragment to the CD44v6 glycopeptide, optionally wherein the binding affinity is measured by surface plasmon resonance, and further optionally where in the surface plasmon resonance is measured in the presence of saturating amounts of either the LAMP1 glycopeptide or the CD44v6 glycopeptide (e.g., about 1 μ M, about 1.5 μ M, or about 2 μ M of either peptide).

477. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 476, which has a binding affinity to the LAMP1 glycopeptide which is at least 100 times the binding affinity of the anti-glyco-LAMP1 antibody or antigen-binding fragment to the CD44v6 glycopeptide, optionally wherein the binding affinity is measured by surface plasmon resonance, and further optionally where in the surface plasmon resonance is

measured in the presence of saturating amounts of either the LAMP1 glycopeptide or the CD44v6 glycopeptide (e.g., about 1 μ M, about 1.5 μ M, or about 2 μ M of either peptide).

478. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 477, which does not specifically bind to the MUC4 peptide CTIPSTAMHTRSTAAPILP (SEQ ID NO:213) that has been glycosylated in vitro with GalNAc on the serine and threonine residues shown with bold and underlined text (the “MUC4 glycopeptide”).

479. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 478, which has a binding affinity to the LAMP1 glycopeptide which is at least 3 times the binding affinity of the anti-glyco-LAMP1 antibody or antigen-binding fragment to the MUC4 glycopeptide, optionally wherein the binding affinity is measured by surface plasmon resonance, and further optionally where in the surface plasmon resonance is measured in the presence of saturating amounts of either the LAMP1 glycopeptide or the MUC4 glycopeptide (e.g., about 1 μ M, about 1.5 μ M, or about 2 μ M of either peptide).

480. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 479, which has a binding affinity to the LAMP1 glycopeptide which is at least 5 times the binding affinity of the anti-glyco-LAMP1 antibody or antigen-binding fragment to the MUC4 glycopeptide, optionally wherein the binding affinity is measured by surface plasmon resonance, and further optionally where in the surface plasmon resonance is measured in the presence of saturating amounts of either the LAMP1 glycopeptide or the MUC4 glycopeptide (e.g., about 1 μ M, about 1.5 μ M, or about 2 μ M of either peptide).

481. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 480, which has a binding affinity to the LAMP1 glycopeptide which is at least 10 times the binding affinity of the anti-glyco-LAMP1 antibody or antigen-binding fragment to the MUC4 glycopeptide, optionally wherein the binding affinity is measured by surface plasmon resonance, and further optionally where in the surface plasmon resonance is measured in the presence of saturating amounts of either the LAMP1 glycopeptide or the MUC4 glycopeptide (e.g., about 1 μ M, about 1.5 μ M, or about 2 μ M of either peptide).

482. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 481, which has a binding affinity to the LAMP1 glycopeptide which is at least 20 times the binding affinity of the anti-glyco-LAMP1 antibody or antigen-binding fragment to the MUC4 glycopeptide, optionally wherein the binding affinity is measured by surface plasmon resonance, and further optionally where in the surface plasmon resonance is measured in the presence of saturating amounts of either the LAMP1 glycopeptide or the MUC4 glycopeptide (e.g., about 1 μ M, about 1.5 μ M, or about 2 μ M of either peptide).

483. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 482, which has a binding affinity to the LAMP1 glycopeptide which is at least 50 times the binding affinity of the anti-glyco-LAMP1 antibody or antigen-binding fragment to

the MUC4 glycopeptide, optionally wherein the binding affinity is measured by surface plasmon resonance, and further optionally where in the surface plasmon resonance is measured in the presence of saturating amounts of either the LAMP1 glycopeptide or the MUC4 glycopeptide (e.g., about 1 μ M, about 1.5 μ M, or about 2 μ M of either peptide).

484. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 483, which has a binding affinity to the LAMP1 glycopeptide which is at least 100 times the binding affinity of the anti-glyco-LAMP1 antibody or antigen-binding fragment to the MUC4 glycopeptide, optionally wherein the binding affinity is measured by surface plasmon resonance, and further optionally where in the surface plasmon resonance is measured in the presence of saturating amounts of either the LAMP1 glycopeptide or the MUC4 glycopeptide (e.g., about 1 μ M, about 1.5 μ M, or about 2 μ M of either peptide).

485. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 484, which does not specifically bind to the cMET peptide PTKSFISGG**ST**ITGVGKNLN (SEQ ID NO:214) that has been glycosylated in vitro with GalNAc on the serine and threonine residues shown with bold and underlined text (the “cMET glycopeptide”).

486. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 485, which has a binding affinity to the LAMP1 glycopeptide which is at least 3 times the binding affinity of the anti-glyco-LAMP1 antibody or antigen-binding fragment to the cMET glycopeptide, optionally wherein the binding affinity is measured by surface plasmon resonance, and further optionally where in the surface plasmon resonance is measured in the presence of saturating amounts of either the LAMP1 glycopeptide or the cMET glycopeptide (e.g., about 1 μ M, about 1.5 μ M, or about 2 μ M of either peptide).

487. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 486, which has a binding affinity to the LAMP1 glycopeptide which is at least 5 times the binding affinity of the anti-glyco-LAMP1 antibody or antigen-binding fragment to the cMET glycopeptide, optionally wherein the binding affinity is measured by surface plasmon resonance, and further optionally where in the surface plasmon resonance is measured in the presence of saturating amounts of either the LAMP1 glycopeptide or the cMET glycopeptide (e.g., about 1 μ M, about 1.5 μ M, or about 2 μ M of either peptide).

488. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 487, which has a binding affinity to the LAMP1 glycopeptide which is at least 10 times the binding affinity of the anti-glyco-LAMP1 antibody or antigen-binding fragment to the cMET glycopeptide, optionally wherein the binding affinity is measured by surface plasmon resonance, and further optionally where in the surface plasmon resonance is measured in the presence of saturating amounts of either the LAMP1 glycopeptide or the cMET glycopeptide (e.g., about 1 μ M, about 1.5 μ M, or about 2 μ M of either peptide).

489. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 488, which has a binding affinity to the LAMP1 glycopeptide which is at least 20 times the binding affinity of the anti-glyco-LAMP1 antibody or antigen-binding fragment to the cMET glycopeptide, optionally wherein the binding affinity is measured by surface plasmon resonance, and further optionally where in the surface plasmon resonance is measured in the presence of saturating amounts of either the LAMP1 glycopeptide or the cMET glycopeptide (e.g., about 1 μ M, about 1.5 μ M, or about 2 μ M of either peptide).

490. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 489, which has a binding affinity to the LAMP1 glycopeptide which is at least 50 times the binding affinity of the anti-glyco-LAMP1 antibody or antigen-binding fragment to the cMET glycopeptide, optionally wherein the binding affinity is measured by surface plasmon resonance, and further optionally where in the surface plasmon resonance is measured in the presence of saturating amounts of either the LAMP1 glycopeptide or the cMET glycopeptide (e.g., about 1 μ M, about 1.5 μ M, or about 2 μ M of either peptide).

491. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 490, which has a binding affinity to the LAMP1 glycopeptide which is at least 100 times the binding affinity of the anti-glyco-LAMP1 antibody or antigen-binding fragment to the cMET glycopeptide, optionally wherein the binding affinity is measured by surface plasmon resonance, and further optionally where in the surface plasmon resonance is measured in the presence of saturating amounts of either the LAMP1 glycopeptide or the cMET glycopeptide (e.g., about 1 μ M, about 1.5 μ M, or about 2 μ M of either peptide).

492. An anti-glyco-LAMP1 antibody or antigen-binding fragment comprising a means for binding a LAMP1 epitope that is overexpressed on cancer cells as compared to normal cells.

493. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 492, wherein the means for binding the LAMP1 epitope comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain.

494. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 493, which is multivalent.

495. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 494, which is an antigen-binding fragment.

496. The anti-glyco-LAMP1 antibody or antigen-binding fragment of embodiment 495, wherein the antigen-binding fragment is in the form of a single-chain variable fragment (scFv).

497. The anti-glyco-LAMP1 antibody or antigen-binding fragment of embodiment 496, wherein the scFv comprises the heavy chain variable fragment N-terminal to the light chain variable fragment.

498. The anti-glyco-LAMP1 antibody or antigen-binding fragment of embodiment 496, wherein the scFv comprises the heavy chain variable fragment C-terminal to the light chain variable fragment.

499. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 496 to 498, wherein the scFv heavy chain variable fragment and light chain variable fragment are covalently bound to a linker sequence, which is optionally 4-15 amino acids.

500. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 494, which is in the form of a multispecific antibody.

501. An anti-glyco-LAMP1 antibody or antigen-binding fragment comprising a means for binding a LAMP1 epitope that is overexpressed on cancer cells as compared to normal cells.

502. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 501, wherein the means for binding the LAMP1 epitope comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain.

503. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 500 to 502, wherein the multispecific antibody is a bispecific antibody that binds to a second epitope that is different from the first epitope.

504. The anti-glyco-LAMP1 antibody or antigen-binding fragment of embodiment 503, wherein the bispecific antibody is a bottle opener, mAb-Fv, mAb-scFv, central-scFv, one-armed central-scFv, or dual scFv format bispecific antibody.

505. The anti-glyco-LAMP1 antibody or antigen-binding fragment of embodiment 504, wherein the bispecific antibody is a bottle opener format bispecific antibody.

506. The anti-glyco-LAMP1 antibody or antigen-binding fragment of embodiment 504, wherein the bispecific antibody is a mAb-Fv format bispecific antibody.

507. The anti-glyco-LAMP1 antibody or antigen-binding fragment of embodiment 504, wherein the bispecific antibody is a mAb-scFv format bispecific antibody.

508. The anti-glyco-LAMP1 antibody or antigen-binding fragment of embodiment 504, wherein the bispecific antibody is a central-scFv format bispecific antibody.

509. The anti-glyco-LAMP1 antibody or antigen-binding fragment of embodiment 504, wherein the bispecific antibody is a one-armed central-scFv format bispecific antibody.

510. The anti-glyco-LAMP1 antibody or antigen-binding fragment of embodiment 504, wherein the bispecific antibody is a dual scFv format bispecific antibody.

511. The anti-glyco-LAMP1 antibody or antigen-binding fragment of embodiment 503, wherein the bispecific antibody is a bispecific domain-exchanged antibody (e.g., a CrossMab), a Fab-arm exchange antibody, a bispecific T-cell engager (BiTE), or a dual-affinity retargeting molecule (DART).

512. The anti-glyco-LAMP1 antibody or antigen-binding fragment of embodiment 511, wherein the bispecific antibody is a bispecific domain-exchanged antibody (e.g., a CrossMab).

513. The anti-glyco-LAMP1 antibody or antigen-binding fragment of embodiment 512, wherein the bispecific antibody is a bispecific IgG comprising a Fab-arm having a domain crossover between heavy and light chains (e.g., a CrossMabFAB).

514. The anti-glyco-LAMP1 antibody or antigen-binding fragment of embodiment 512, wherein the bispecific antibody is a bispecific IgG comprising a Fab-arm having a domain crossover between variable heavy and variable light chains (e.g., a CrossMabVH-VL).

515. The anti-glyco-LAMP1 antibody or antigen-binding fragment of embodiment 512, wherein the bispecific antibody is a bispecific IgG comprising a Fab-arm having a domain crossover between constant heavy and constant light chains (e.g., a CrossMabCH1-CL).

516. The anti-glyco-LAMP1 antibody or antigen-binding fragment of embodiment 511, wherein the bispecific antibody is a Fab-arm exchange antibody.

517. The anti-glyco-LAMP1 antibody or antigen-binding fragment of embodiment 511, wherein the bispecific antibody is a dual-affinity retargeting molecule (DART).

518. The anti-glyco-LAMP1 antibody or antigen-binding fragment of embodiment 511, wherein the bispecific antibody is a bispecific T-cell engager (BiTE).

519. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 503 to 518, wherein the second epitope is a LAMP1 epitope.

520. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 503 to 518, wherein the second epitope is a LAMP1 epitope that is overexpressed on cancer cells as compared to normal cells.

521. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 503 to 518, wherein the second epitope is a T-cell epitope.

522. The anti-glyco-LAMP1 antibody or antigen-binding fragment of embodiment 521, wherein the T-cell epitope comprises a CD3 epitope, a CD8 epitope, a CD16 epitope, a CD25 epitope, a CD28 epitope, or an NKG2D epitope.

523. The anti-glyco-LAMP1 antibody or antigen-binding fragment of embodiment 522, wherein the T-cell epitope comprises a CD3 epitope, which is optionally an epitope present in human CD3.

524. The anti-glyco-LAMP1 antibody or antigen-binding fragment of embodiment 523, wherein the CD3 epitope comprises a CD3 gamma epitope, a CD3 delta epitope, a CD3 epsilon epitope, or a CD3 zeta epitope.

525. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of embodiments 1 to 524 which is conjugated to a detectable moiety.

526. The anti-glyco-LAMP1 antibody or antigen binding fragment of embodiment 525 in which the detectable moiety is an enzyme, a radioisotope, or a fluorescent label.

527. A bispecific antibody comprising (a) a means for binding a LAMP1 epitope that is overexpressed on cancer cells as compared to normal cells and (b) a means for binding a T-cell epitope, optionally wherein the bispecific antibody has the features described in any one of embodiments 503 to 526.

528. The bispecific antibody of embodiment 527, wherein the means for binding the LAMP1 epitope comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain.

529. The bispecific antibody of embodiment 527 or embodiment 528, wherein the means for binding the T-cell epitope comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain.

530. The bispecific antibody of any one of embodiments 527 to 529, wherein the T-cell epitope comprises a CD3 epitope, a CD8 epitope, a CD16 epitope, a CD25 epitope, a CD28 epitope, or an NKG2D epitope.

531. The bispecific antibody of embodiment 530, wherein the T-cell epitope comprises a CD3 epitope, which is optionally an epitope present in human CD3.

532. The bispecific antibody of embodiment 531, wherein the CD3 epitope comprises a CD3 gamma epitope, a CD3 delta epitope, a CD3 epsilon epitope, or a CD3 zeta epitope.

533. A fusion protein comprising the amino acid sequence of the anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 526 or the bispecific antibody of any one of embodiments 527 to 532, operably linked to at least a second amino acid sequence.

534. The fusion protein of embodiment 533, wherein the second amino acid sequence is that of 4-1BB, CD2, CD3-zeta, or a fragment thereof.

535. The fusion protein of embodiment 533, wherein the second amino acid sequence is that of a fusion peptide.

536. The fusion protein of embodiment 535, wherein the fusion peptide is a CD28-CD3-zeta, a 4-1BB (CD137)-CD3-zeta fusion peptide, a CD2-CD3-zeta fusion peptide, a CD28-CD2-CD3-zeta fusion peptide, or a 4-1BB (CD137)-CD2-CD3-zeta fusion peptide.

537. The fusion protein of embodiment 533, wherein the second amino acid sequence is that of a modulator of T cell activation or a fragment thereof.

538. The fusion protein of embodiment 537, wherein the modulator of T cell activation is IL-15 or IL-15R α .

539. The fusion protein of embodiment 533, wherein the second amino acid sequence is that of a MIC protein domain.

540. The fusion protein of embodiment 539, wherein the MIC protein domain is an α 1- α 2 domain.

541. The fusion protein of embodiment 540, wherein the α 1- α 2 domain is a MICA, MICB, ULBP1, ULBP2, ULBP3, ULBP4, ULBP5, ULBP6, or OMCP α 1- α 2 domain.

542. The fusion protein of any one of embodiments 539 to 541, wherein the MIC protein domain is an engineered MIC protein domain.

543. The fusion protein of embodiment 533, wherein the second amino acid sequence is that of a neuraminidase (EC 3.2.1.18 or EC 3.2.1.129).

544. The fusion protein of embodiment 543, wherein the neuraminidase amino acid sequence is derived from *Micromonospora viridifaciens*.

545. The fusion protein of embodiment 543 or 544, wherein the neuraminidase comprises an amino acid sequence having at least 95% sequence identity to
GGSPVPPGGEPLYTEQDLAVNGREGFPNYRIPALTVTPDGDLLASYDGRPTGIDAPGPNSILQ
RRSTDGGRTWGEQQVVSAGQTTAPIKGFSDPSYLVRETGTIFNFHVYSQRQGFAGSRPGTD
PADPNVLHANVATSTDGGLTWSHRTITADITPDGWRSRFAASGEGIQRLRYGPHAGRLIQYTI
INAAGAFQAVSVYSDDHGRTWRAGEAVGVGMDENKTVELSDGRVLLNSRDSARSGYRKVAV
STDGGHSYGPVTIDRDLPDPTNNASIIRAFPDAPAGSARAKVLLFSNAASQTSRSQGTIRMSCD
DGQTWPVSKVFQPGSMSYSTLTALPDGTYGLLYEPGTGIRYANFNLAWLGG (SEQ ID
NO:210).

546. The fusion protein of any one of embodiments 543 to 545, wherein the neuraminidase comprises an amino acid sequence having at least 97% sequence identity to
GGSPVPPGGEPLYTEQDLAVNGREGFPNYRIPALTVTPDGDLLASYDGRPTGIDAPGPNSILQ
RRSTDGGRTWGEQQVVSAGQTTAPIKGFSDPSYLVRETGTIFNFHVYSQRQGFAGSRPGTD
PADPNVLHANVATSTDGGLTWSHRTITADITPDGWRSRFAASGEGIQRLRYGPHAGRLIQYTI
INAAGAFQAVSVYSDDHGRTWRAGEAVGVGMDENKTVELSDGRVLLNSRDSARSGYRKVAV
STDGGHSYGPVTIDRDLPDPTNNASIIRAFPDAPAGSARAKVLLFSNAASQTSRSQGTIRMSCD
DGQTWPVSKVFQPGSMSYSTLTALPDGTYGLLYEPGTGIRYANFNLAWLGG (SEQ ID
NO:210).

547. The fusion protein of any one of embodiments 543 to 546, wherein the neuraminidase comprises an amino acid sequence having at least 98% sequence identity to
GGSPVPPGGEPLYTEQDLAVNGREGFPNYRIPALTVTPDGDLLASYDGRPTGIDAPGPNSILQ
RRSTDGGRTWGEQQVVSAGQTTAPIKGFSDPSYLVRETGTIFNFHVYSQRQGFAGSRPGTD
PADPNVLHANVATSTDGGLTWSHRTITADITPDGWRSRFAASGEGIQRLRYGPHAGRLIQYTI
INAAGAFQAVSVYSDDHGRTWRAGEAVGVGMDENKTVELSDGRVLLNSRDSARSGYRKVAV
STDGGHSYGPVTIDRDLPDPTNNASIIRAFPDAPAGSARAKVLLFSNAASQTSRSQGTIRMSCD
DGQTWPVSKVFQPGSMSYSTLTALPDGTYGLLYEPGTGIRYANFNLAWLGG (SEQ ID
NO:210).

548. The fusion protein of any one of embodiments 543 to 547, wherein the neuraminidase comprises an amino acid sequence having at least 99% sequence identity to
GGSPVPPGGEPLYTEQDLAVNGREGFPNYRIPALTVTPDGDLLASYDGRPTGIDAPGPNSILQ
RRSTDGGRTWGEQQVVSAGQTTAPIKGFSDPSYLVRETGTIFNFHVYSQRQGFAGSRPGTD
PADPNVLHANVATSTDGGLTWSHRTITADITPDGWRSRFAASGEGIQRLRYGPHAGRLIQYTI

INAAGAFQAVSVYSDDHGRTWRAGEAVGVGMDENKTVELSDGRVLLNSRDSARSGYRKVAV
 STDGGHSYGPVTIDRDLPDPTNNASIIRAFPDAPAGSARAKVLLFSNAASQTSRSQGTIRMSCD
 DGQTWPVSKVFQPGSMSYSTLTALPDGTYGLLYEPGTGIRYANFNLAWLGG (SEQ ID
 NO:210).

549. The fusion protein of any one of embodiments 543 to 548, wherein the neuraminidase comprises the amino acid
 GGSPVPPGGEPLYTEQDLAVNGREGFPNYRIPALTVTPDGDLLASYDGRPTGIDAPGPNSILQ
 RRSTDGGRTWGEQQVWSAGQTTAPIKGFSDPSYLVRETGTIFNFHVYSQRQGFAGSRPGTD
 PADPNVLHANVATSTDGGLTWSHRTITADITPDGWRSRFAASGEGIQLRYGPHAGRLIQQYTI
 INAAGAFQAVSVYSDDHGRTWRAGEAVGVGMDENKTVELSDGRVLLNSRDSARSGYRKVAV
 STDGGHSYGPVTIDRDLPDPTNNASIIRAFPDAPAGSARAKVLLFSNAASQTSRSQGTIRMSCD
 DGQTWPVSKVFQPGSMSYSTLTALPDGTYGLLYEPGTGIRYANFNLAWLGG (SEQ ID
 NO:210).

550. The fusion protein of any one of embodiments 543 to 549, which comprises a signal sequence.

551. The fusion protein of embodiment 550, wherein the signal sequence is a granulysin signal sequence.

552. The fusion protein of embodiment 550, wherein the signal sequence is a granzymeK signal sequence.

553. The fusion protein of embodiment 550, wherein the signal sequence is an NPY signal sequence.

554. The fusion protein of embodiment 550, wherein the signal sequence is an IFN signal sequence.

555. The fusion protein of any one of embodiments 543 to 554, which comprises a self-cleaving peptide sequence.

556. The fusion protein of embodiment 555, wherein the self-cleaving peptide sequence is a 2A peptide.

557. The fusion protein of embodiment 556, wherein the 2A peptide is T2A.

558. A chimeric antigen receptor (CAR) comprising one or more antigen-binding fragments according to any one of embodiments 495 to 499.

559. The CAR of embodiment 558, which comprises one or more scFvs according to any one of embodiments 496 to 499.

560. The CAR of embodiment 559, which comprises one scFv according to any one of embodiments 496 to 499.

561. The CAR of embodiment 560, which comprises two scFvs according to any one of embodiments 496 to 499.

562. The CAR of embodiment 561, wherein the two scFvs have the same amino acid sequence.

563. The CAR of embodiment 561 or 562, wherein the two scFvs are covalently bound by a linker sequence, which is optionally 4-15 amino acids.

564. The CAR of any one of embodiments 543 to 563, comprising in amino- to carboxy-terminal order: (i) the one or more antigen-binding fragments, (ii) a transmembrane domain, and (iii) an intracellular signaling domain.

565. A chimeric antigen receptor (CAR) comprising in amino- to carboxy-terminal order: (i) one or more means for binding a LAMP1 epitope that is overexpressed on cancer cells as compared to normal cells, (ii) a transmembrane domain, and (iii) an intracellular signaling domain.

566. The CAR of embodiment 565, wherein the means for binding the LAMP1 epitope comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain.

567. The CAR of any one of embodiments 564 to 566, wherein the transmembrane domain comprises a CD28 transmembrane domain.

568. The CAR of embodiment 567, wherein the CD28 transmembrane domain comprises the amino acid sequence FWVLVVVGGVLACYSLLVTVAFIIFWV (SEQ ID NO: 163).

569. The CAR of any one of embodiments 564 to 568, wherein the intracellular signaling domain comprises a co-stimulatory signaling region.

570. The CAR of embodiment 569, wherein the co-stimulatory signaling region comprises a signaling portion of, or the entire, cytoplasmic domain of CD27, CD28, 4-1BB, OX40, CD30, CD40, PD-1, ICOS, lymphocyte function-associated antigen-1 (LFA-1), CD2, CD7, LIGHT, NKG2C, B7-H3, a ligand that specifically binds with CD83, DAP10, GITR, or a combination thereof.

571. The CAR of embodiment 570, wherein the CD27, CD28, 4-1BB, OX40, CD30, CD40, PD-1, ICOS, lymphocyte function-associated antigen-1 (LFA-1), CD2, CD7, LIGHT, NKG2C, B7-H3, a ligand that specifically binds with CD83, DAP10, or GITR a human CD27, CD28, 4-1BB, OX40, CD30, CD40, PD-1, ICOS, lymphocyte function-associated antigen-1 (LFA-1), CD2, CD7, LIGHT, NKG2C, B7-H3, a ligand that specifically binds with CD83, DAP10, or GITR.

572. The CAR of embodiment 570 or embodiment 571, wherein a signaling portion of, or the entire co-stimulatory signaling domain comprises the cytoplasmic domain of CD2.

573. The CAR of embodiment 572, wherein the cytoplasmic domain of CD2 comprises the amino acid sequence
TKRKKQRSRRNDEELETRAHRVATEERGRKPHQIPASTPQNPATSQHPPPPPGHRSQAPSHR
PPPPGHRVQHQPQKRPPAPSGTQVHQKGPPLPRPRVQPKPPHGAAENSLSPSSN (SEQ ID NO:170).

574. The CAR of any one of embodiments 570 to 573, wherein the co-stimulatory signaling domain comprises a signaling portion of, or the entire, cytoplasmic domain of CD28.

575. The CAR of embodiment 574, wherein the cytoplasmic domain of CD28 comprises the amino acid sequence
RSKRSRLLHSDYMNMTPRRPGPTRKHYQPYAPPRDFAAYRS (SEQ ID NO:169).

576. The CAR of any one of embodiments 563 to 575, wherein the intracellular signaling domain comprises a T cell signaling domain.

577. The CAR of embodiment 576, wherein the T cell signaling domain is C-terminal to the co-stimulatory signaling region.

578. The CAR of embodiment 576 or embodiment 577, wherein the T cell signaling domain comprises a CD3-zeta signaling domain.

579. The CAR of embodiment 578, wherein the CD3-zeta signaling domain comprises the amino acid sequence
RVKFSRSADAPAYQQGQNQLYNELNLGRREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYN
ELQKDKMAEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQALPPR (SEQ ID NO: 168).

580. The CAR of any one of embodiments 564 to 579, which further comprises a signal peptide N-terminal to the one or more antibody fragments, one or more scFvs, or one or more means for binding a LAMP1 epitope.

581. The CAR of embodiment 579, wherein the signal peptide is a human CD8 signal peptide.

582. The CAR of embodiment 581, wherein the human CD8 signal peptide comprises the amino acid sequence MALPVTALLLPLALLLHAARP (SEQ ID NO:161).

583. The CAR of any one of embodiments 564 to 582, which further comprises a hinge between the one or more antigen-binding fragments and the transmembrane domain.

584. The CAR of embodiment 583, wherein the hinge comprises a human CD8a hinge.

585. The CAR of embodiment 584, wherein the human CD8a hinge comprises the amino acid sequence TTPAPRPPTPAPTIASPLSLRPEACRPAAGGAVHTRGLDFAC (SEQ ID NO: 165).

586. The CAR of embodiment 584, wherein the human CD8a hinge comprises the amino acid sequence TTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACD (SEQ ID NO:220).

587. The CAR of embodiment 583, wherein the hinge comprises a human IgG4-short hinge comprising the amino acid sequence ESKYGPPCPSCP (SEQ ID NO:166).

588. The CAR of embodiment 583, wherein the hinge comprises a human IgG4-long hinge comprising the amino acid sequence
ESKYGPPCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDG
VEVHNAKTKPREEQFQSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPR

EPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLY
SRLTVDKSRWQEGNVFSCSVMHEALHNHYTQKSLSLGLGKM (SEQ ID NO: 167).

589. A chimeric antigen receptor (CAR), whose amino acid sequence comprises the amino acid sequence of 3C7-CART of Table 14 (SEQ ID NO: 205).

590. A chimeric antigen receptor (CAR), whose amino acid sequence comprises the amino acid sequence of 13C3-CART of Table 14 (SEQ ID NO: 206).

591. A chimeric antigen receptor (CAR), whose amino acid sequence comprises the amino acid sequence of 13G2-CART of Table 14 (SEQ ID NO: 207).

592. An antibody-drug conjugate comprising the anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 526 or the fusion protein of any one of embodiments 527 to 557 conjugated to a cytotoxic agent.

593. The antibody-drug conjugate of embodiment 592, wherein the cytotoxic agent is an auristatin, a DNA minor groove binding agent, an alkylating agent, an enediyne, a lexitropsin, a duocarmycin, a taxane, a dolastatin, a maytansinoid, or a vinca alkaloid.

594. The antibody-drug conjugate of embodiment 593, wherein the anti-glyco-LAMP1 antibody or antigen-binding fragment or bispecific antibody is conjugated to the cytotoxic agent via a linker.

595. The antibody-drug conjugate of embodiment 594, wherein the linker is cleavable under intracellular conditions.

596. The antibody-drug conjugate of embodiment 595, wherein the cleavable linker is cleavable by an intracellular protease.

597. The antibody-drug conjugate of embodiment 596, wherein the linker comprises a dipeptide.

598. The antibody-drug conjugate of embodiment 597, wherein the dipeptide is val-cit or phe-lys.

599. The antibody-drug conjugate of embodiment 595, wherein the cleavable linker is hydrolyzable at a pH of less than 5.5.

600. The antibody-drug conjugate of embodiment 599, wherein the hydrolyzable linker is a hydrazone linker.

601. The antibody-drug conjugate of embodiment 595, wherein the cleavable linker is a disulfide linker.

602. A chimeric T cell receptor (TCR) comprising

- (a) an antigen-binding fragment according to any one of embodiments 495 to 499
- (b) a first polypeptide chain comprising a first TCR domain comprising a first TCR transmembrane domain from a first TCR subunit; and

- (c) a second polypeptide chain comprising a second TCR domain comprising a second TCR transmembrane domain from a second TCR subunit.

603. The chimeric TCR of embodiment 602, which comprises one or more scFvs according to any one of embodiments 496 to 499.

604. The chimeric TCR of embodiment 602 or 563, which comprises one scFv according to any one of embodiments 496 to 499.

605. A chimeric T cell receptor (TCR) comprising:

- (a) a means for binding a LAMP1 epitope that is overexpressed on cancer cells as compared to normal cells;
- (b) a first polypeptide chain comprising a first TCR domain comprising a first TCR transmembrane domain from a first TCR subunit; and
- (c) a second polypeptide chain comprising a second TCR domain comprising a second TCR transmembrane domain from a second TCR subunit.

606. The chimeric TCR of embodiment 605, wherein the means for binding a LAMP1 epitope that is overexpressed on cancer cells as compared to normal cells comprises an scFv.

607. The chimeric TCR of embodiment 604 or 606, wherein the first polypeptide chain further comprises the scFv, and optionally further comprises a linker between the first TCR domain and the scFv.

608. The chimeric TCR of embodiment 604 or 606, wherein the second polypeptide chain further comprises the scFv, and optionally further comprises a linker between the second TCR domain and the scFv.

609. The chimeric TCR of embodiment 602 or 603, which comprises two scFvs according to any one of embodiments 496 to 499.

610. The chimeric TCR of embodiment 605, wherein the means for binding a LAMP1 epitope that is overexpressed on cancer cells as compared to normal cells comprises two scFvs.

611. The chimeric TCR of embodiment 609 or 610, wherein the two scFvs have the same amino acid sequence.

612. The chimeric TCR of embodiment 609 or 610, wherein the two scFvs have different amino acid sequences.

613. The chimeric TCR of any one of embodiments 609 to 612, wherein the two scFvs are covalently bound by a linker sequence, which is optionally 4-15 amino acids in length.

614. The chimeric TCR of any one of embodiments 609 to 613, wherein the first polypeptide chain further comprises the two scFvs, and optionally further comprises a linker between the first TCR domain and a first scFv of the two scFvs.

615. The chimeric TCR of any one of embodiments 609 to 613, wherein the second polypeptide chain further comprises the two scFvs, and optionally further comprises a linker between the second TCR domain and a first scFv of the two scFvs.

616. The chimeric TCR of any one of embodiments 609 to 613, wherein the first polypeptide chain comprises a first scFv of the two scFvs, and the second polypeptide chain comprises a second scFv of the two scFvs, and optionally wherein (i) the first polypeptide chain comprises a first linker between the first TCR domain and the first scFv, and (ii) the second polypeptide chain comprises a second linker between the second TCR domain and the second scFv.

617. The chimeric TCR of embodiment 602, wherein the antigen-binding fragment is an anti-glyco-LAMP1 Fv fragment.

618. The chimeric TCR of embodiment 605, wherein the means for binding a LAMP1 epitope that is overexpressed on cancer cells as compared to normal cells is an anti-glyco-LAMP1 Fv fragment.

619. The chimeric TCR of embodiment 617 or 618, wherein the Fv fragment comprises an anti-glyco-LAMP1 variable heavy chain (VH) and an anti-glyco-LAMP1 variable light chain (VL), optionally wherein the VH and VL are a VH and a VL of an anti-glyco-LAMP1 antibody or binding fragment according to any one of embodiments 1 to 526.

620. The chimeric TCR of embodiment 619, wherein the first polypeptide chain further comprises the anti-glyco-LAMP1 VH and the second polypeptide chain further comprises the anti-glyco-LAMP1 VL, optionally wherein (i) the first polypeptide chain further comprises a linker between the first TCR domain and the anti-glyco-LAMP1 VH, and (ii) the second polypeptide chain further comprises a linker between the second TCR domain and the anti-glyco-LAMP1 VL.

621. The chimeric TCR of embodiment 619, wherein the first polypeptide chain further comprises the anti-glyco-LAMP1 VL and the second polypeptide chain further comprises the anti-glyco-LAMP1 VH, optionally wherein (i) the first polypeptide chain further comprises a linker between the first TCR domain and the anti-glyco-LAMP1 VL, and (ii) the second polypeptide chain further comprises a linker between the second TCR domain and the anti-glyco-LAMP1 VH.

622. The chimeric TCR of any one of embodiments 602 and 617 to 621, wherein the first polypeptide chain further comprises a common heavy chain 1 (CH1) domain.

623. The chimeric TCR of any one of embodiments 602 and 617 to 622, wherein the second polypeptide chain further comprises a common light chain (CL) domain.

624. The chimeric TCR of embodiment 602, wherein the antigen-binding fragment is an anti-glyco-LAMP1 Fab domain.

625. The chimeric TCR of embodiment 605, wherein the means for binding a LAMP1 epitope that is overexpressed on cancer cells as compared to normal cells is an anti-glyco-LAMP1 Fab domain.

626. The chimeric TCR of embodiment 624 or 625, which comprises one anti-glyco-LAMP1 Fab domain.

627. The chimeric TCR of embodiment 624 or 625, which comprises two anti-glyco-LAMP1 Fab domain.

628. The chimeric TCR of embodiment 627, wherein the two Fab domains have the same amino acid sequence.

629. The chimeric TCR of embodiment 627, wherein the two Fab domains have different amino acid sequences.

630. The chimeric TCR of any one of embodiments 624 to 629, wherein the Fab domain or each Fab domain comprises an anti-glyco-LAMP1 variable heavy chain (VH) and an anti-glyco-LAMP1 variable light chain (VL), optionally wherein the VH and VL are a VH and a VL of an anti-glyco-LAMP1 antibody or binding fragment according to any one of embodiments 1 to 526.

631. The chimeric TCR of embodiment 630, wherein the first polypeptide chain comprises the anti-glyco-LAMP1 VH and a CH1 domain or a CL domain, optionally wherein the first polypeptide chain comprises a linker between the first TCR domain and the CH1 domain or the CL domain.

632. The chimeric TCR of embodiment 631, wherein the second polypeptide chain comprises the anti-glyco-LAMP1 VL and a CL domain or a CH1 domain, optionally wherein the second polypeptide chain comprises a linker between the second TCR domain and the CL domain or the CH1 domain.

633. The chimeric TCR of embodiment 631, comprising a third polypeptide chain comprising the anti-glyco-LAMP1 VL and a CL domain or a CH1 domain, the third polypeptide chain being capable of associating with the anti-glyco-LAMP1 VH and the CH1 domain or the CL domain of the first polypeptide chain.

634. The chimeric TCR of embodiment 630, wherein the second polypeptide chain comprises the anti-glyco-LAMP1 VH and a CH1 domain or a CL domain, optionally wherein the second polypeptide chain comprises a linker between the second TCR domain and the CH1 domain or the CL domain.

635. The chimeric TCR of embodiment 634, wherein the first polypeptide chain comprises the anti-glyco-LAMP1 VL and a CL or a CH1 domain, optionally wherein the first polypeptide chain comprises a linker between the second TCR domain and the CL domain or the CH1.

636. The chimeric TCR of embodiment 634, comprising a third polypeptide chain comprising the anti-glyco-LAMP1 VL and a CL domain or a CH1 domain, the third polypeptide

chain being capable of associating with the anti-glyco-LAMP1 VH and the CH1 domain or the CL domain of the second polypeptide chain.

637. The chimeric TCR of embodiment 630, wherein the first polypeptide chain comprises a first anti-glyco-LAMP1 VH and a first chain CH1 domain or a first chain CL domain and the second polypeptide chain comprises a second anti-glyco-LAMP1 VH and a second chain CH1 domain or a second chain CL domain, optionally wherein the first polypeptide chain comprises a linker between the first TCR domain and the first chain CH1 domain or the first chain CL domain, and optionally wherein the second polypeptide chain comprises a linker between the second TCR domain and the second chain CH1 domain or the second chain CL domain.

638. The chimeric TCR of embodiment 637, comprising:

- (a) a third polypeptide chain comprising a first anti-glyco-LAMP1 VL and a third chain CL domain or a third chain CH1 domain, capable of associating with the first anti-glyco-LAMP1 VH and the first chain CH1 domain or the first chain CL domain of the first polypeptide; and
- (b) a fourth polypeptide chain comprising a second anti-glyco-LAMP1 VL and a fourth chain CL domain or a fourth chain CH1 domain, capable of associating with the second anti-glyco-LAMP1 VH and the second chain CH1 domain or the second chain CL domain of the second polypeptide.

639. The chimeric TCR of any one of embodiments 602 to 638, when depending directly or indirectly from embodiment 576, wherein the antigen-binding fragment comprises an anti-glyco-LAMP1 variable heavy chain comprising the amino acid sequence of EVKLEESGGGLVQPGGSMKVSCGASGFTFSDAWMDWVRQSPEKGLEWVAEMRSKAFNHAIYYAESVKGRFTISRDDSKSRVYLQMNLLRPEDTGIYYCTPNWDEGFAYWGQGTTLVTVSA (SEQ ID NO: 1).

640. The chimeric TCR of any one of embodiments 602 to 638 when depending directly or indirectly from embodiment 576, wherein the antigen-binding fragment comprises an anti-glyco-LAMP1 variable heavy chain comprising the amino acid sequence of EVKLEDGGGLVQPGGSMKLSCAASGFTFSDAWMDWVRHSPEKGLEWVAELRSKAFNHATYYAESVKGRFTISRDDSKSTVYLQMNSLRAEDTGIYYCTPNWDEGFAYWGQGTTLVTVSA (SEQ ID NO: 23).

641. The chimeric TCR of any one of embodiments 602 to 638, when depending directly or indirectly from embodiment 576, wherein the antigen-binding fragment comprises an anti-glyco-LAMP1 variable heavy chain comprising the amino acid sequence of EVRLEESGGGLVQPGGSMKLSCVASGFTFSDAWMDWVRQSPERGLEWVAELRSKTFNHATYYAESVRGRFTISRDDSKSTVYLQMNSLRAEDTGIYYCSPNWDEGFAYWGQGTTLVTVSA (SEQ ID NO: 45).

642. The chimeric TCR of any one of embodiments 602 to 638, when depending directly or indirectly from embodiment 576, wherein the antigen-binding fragment comprises an anti-glyco-LAMP1 variable heavy chain comprising the amino acid sequence of EVQLLES GGGLVQP GGSLRLSCAASGFTFSDAWMDWVRHAPGKGLEWVAELRSKAFNHATY YAESVKGRFTISRDDSKNTVYLQMNSLRAEDTAVYYCTPNWDEGFAYWGQGTLVTVSS (SEQ ID NO: 133).

643. The chimeric TCR of any one of embodiments 602 to 638, when depending directly or indirectly from embodiment 576, wherein the antigen-binding fragment comprises an anti-glyco-LAMP1 variable heavy chain comprising the amino acid sequence of EVQLLES GGGLVQP GGSLRLSCAASGFTFSDAWMDWVRQAPGKGLEWVSELRSKAFNHATY YAESVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCTPNWDEGFAYWGQGTLVTVSS (SEQ ID NO: 134).

644. The chimeric TCR of any one of embodiments 602 to 638, when depending directly or indirectly from embodiment 576, wherein the antigen-binding fragment comprises an anti-glyco-LAMP1 variable heavy chain comprising the amino acid sequence of EVQLLES GGGLVQP GGSLRLSCAASGFTFSDAWMDWVRQAPGKGLEWVSEIRSSAFNHATY YAESVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCTPNWDEGFAYWGQGTLVTVSS (SEQ ID NO: 135).

645. The chimeric TCR of any one of embodiments 602 to 638, when depending directly or indirectly from embodiment 576, wherein the antigen-binding fragment comprises an anti-glyco-LAMP1 variable heavy chain comprising the amino acid sequence of EVQLVES GGGLVKP GGSLRLSCAASGFTFSDAWMDWVRHAPGKGLEWVAELRSKAFNHATY YAESVKGRFTISRDDSKNTVYLQMNSLKTEDTAVYYCTPNWDEGFAYWGQGTLVTVSS (SEQ ID NO: 136).

646. The chimeric TCR of any one of embodiments 602 to 638, when depending directly or indirectly from embodiment 576, wherein the antigen-binding fragment comprises an anti-glyco-LAMP1 variable heavy chain comprising the amino acid sequence of EVQLVES GGGLVKP GGSLRLSCAASGFTFSDAWMDWVRQAPGKGLEWVGELRSKAFNHAT YYAESVKGRFTISRDDSKNTLYLQMNSLKTEDTAVYYCTPNWDEGFAYWGQGTLVTVSS (SEQ ID NO: 137).

647. The chimeric TCR of any one of embodiments 602 to 638, when depending directly or indirectly from embodiment 576, wherein the antigen-binding fragment comprises an anti-glyco-LAMP1 variable heavy chain comprising the amino acid sequence of EVQLVES GGGLVKP GGSLRLSCAASGFTFSDAWMDWVRQAPGKGLEWVGEIRSKAFNHATY YAE PVKGRFTISRDDSKNTLYLQMNSLKTEDTAVYYCTPNWDEGFAYWGQGTLVTVSS (SEQ ID NO: 138).

648. The chimeric TCR of any one of embodiments 602 to 638, when depending directly or indirectly from embodiment 576, wherein the antigen-binding fragment comprises an

anti-glyco-LAMP1 variable heavy chain comprising the amino acid sequence of EVQLVESGGGLVQPGGSLRLSCAASGFTFSDAWMDWVRHAPGKGLEWVAELRSKAFNHATY YAESVKGRFTISRDDSKNSVYLQMNSLKTEDTAVYYCTPNWDEGFAYWGQGLTVTVSS (SEQ ID NO: 139).

649. The chimeric TCR of any one of embodiments 602 to 638, when depending directly or indirectly from embodiment 576, wherein the antigen-binding fragment comprises an anti-glyco-LAMP1 variable heavy chain comprising the amino acid sequence of EVQLVESGGGLVQPGGSLRLSCAASGFTFSDAWMDWVRQAPGKGLEWVGELRSKAFNHAT YYAESVKGRFTISRDDSKNSLYLQMNSLKTEDTAVYYCTPNWDEGFAYWGQGLTVTVSS (SEQ ID NO: 140).

650. The chimeric TCR of any one of embodiments 602 to 638, when depending directly or indirectly from embodiment 576, wherein the antigen-binding fragment comprises an anti-glyco-LAMP1 variable heavy chain comprising the amino acid sequence of EVQLVESGGGLVQPGGSLRLSCAASGFTFSDAWMDWVRQAPGKGLEWVGELRSKAFNYAT YYAESVKGRFTISRDDSKNSLYLQMNSLKTEDTAVYYCTPNWDEGFAYWGQGLTVTVSS (SEQ ID NO: 141).

651. The chimeric TCR of any one of embodiments 602 to 638, when depending directly or indirectly from embodiment 576, wherein the antigen-binding fragment comprises an anti-glyco-LAMP1 variable heavy chain comprising the amino acid sequence of QVQLVQSGSELKKPGASVKVSKASGFTFSDAWMDWVRHAPGQGLEWVAELRSKAFNHAT YYAESVKGRFVISRDDSVSTVYLQISSLKAEDTAVYYCTPNWDEGFAYWGQGLTVTVSS (SEQ ID NO: 142).

652. The chimeric TCR of any one of embodiments 602 to 638, when depending directly or indirectly from embodiment 576, wherein the antigen-binding fragment comprises an anti-glyco-LAMP1 variable heavy chain comprising the amino acid sequence of QVQLVQSGSELKKPGASVKVSKASGYTFSDAWMDWVRQAPGQGLEWMGELRSKAFNHAT YYAESVKGRFVISRDDSVSTAYLQISSLKAEDTAVYYCAPNWDEGFAYWGQGLTVTVSS (SEQ ID NO: 143).

653. The chimeric TCR of any one of embodiments 602 to 638, when depending directly or indirectly from embodiment 576, wherein the antigen-binding fragment comprises an anti-glyco-LAMP1 variable heavy chain comprising the amino acid sequence of QVQLVQSGSELKKPGASVKVSKASGYTFTSAWMNWVRQAPGQGLEWMGEIRTNFNAFHAP YYAQGVKGRFVISRDDSVSTAYLQISSLKAEDTAVYYCAPNWDEGFAYWGQGLTVTVSS (SEQ ID NO: 144).

654. The chimeric TCR of any one of embodiments 602 to 638, when depending directly or indirectly from embodiment 576, wherein the antigen-binding fragment comprises an anti-glyco-LAMP1 variable heavy chain comprising:

- (a) a complementarity determining region (CDR) H1 comprising the amino acid sequence of GFTFSDAW (SEQ ID NO:67), DAWMD (SEQ ID NO:73), GFTFSDA (SEQ ID NO:79), GFTFSDAWMD (SEQ ID NO:103), or DA (SEQ ID NO:127);
- (b) a CDR-H2 comprising the amino acid sequence of X₁RSKX₂FNHAX₃ (SEQ ID NO:68), EX₁RSKX₂FNHAX₃YYAESVX₄G (SEQ ID NO:74), RSKX₂FNHA (SEQ ID NO:80), or SKX₂FNHA (SEQ ID NO:128); and
- (c) a CDR-H3 comprising the amino acid sequence of X₅PNWDEGFAY (SEQ ID NO:69), or NWDEGFAY (SEQ ID NO: 75).

655. The chimeric TCR of any one of embodiments 602 to 654 when depending directly or indirectly from embodiment 576, wherein the antigen-binding fragment comprises an anti-glyco-LAMP1 variable light chain comprising the amino acid sequence of DVMLTQTPLSLPVSLGDQASISCRSSQSLVHSNGNTYLHWYLQKPGQSPKLLINKVSNRFFGV PDRFSGSGSGTDFTLKISRVEAEDLGVYFCSQSTHVPRTFGGGTKLEIK (SEQ ID NO: 2).

656. The chimeric TCR of any one of embodiments 602 to 654 when depending directly or indirectly from embodiment 576, wherein the antigen-binding fragment comprises an anti-glyco-LAMP1 variable light chain comprising the amino acid sequence of NIMMTQSPSSLVVSAGEKVTMSCKSSHSVLYSSNQKNYLAWYQQKPGQSPKLLIYWASTKNS GVPDRFTGSGSGTDFTLTISVQAEDLAVYYCHQYLSSYTFGGGTKLEIK (SEQ ID NO: 24).

657. The chimeric TCR of any one of embodiments 602 to 654 when depending directly or indirectly from embodiment 576, wherein the antigen-binding fragment comprises an anti-glyco-LAMP1 variable light chain comprising the amino acid sequence of DVVMTQIPLSLCVSLGDQASISCRSSQSLVHNNGNTYLHWYLQKPGQSPKLLINKVSKRFTGV PDRFSGSGSGTDFTLKISRVEAEDLGVYFCSQSTHVPRTFGGGTKLEIK (SEQ ID NO: 46).

658. The chimeric TCR of any one of embodiments 602 to 654 when depending directly or indirectly from embodiment 576, wherein the antigen-binding fragment comprises an anti-glyco-LAMP1 variable light chain comprising the amino acid sequence of DVVMTQSPLSLPVTLGQPASISCRSSQSLVHSNGNTYLHWYQQRPQGQSPRLLINKVSNRFSG VPDRFSGSGSGTDFTLKISRVEAEDVGVYFCSQSTHVPRTFGGGTKVEIK (SEQ ID NO: 145).

659. The chimeric TCR of any one of embodiments 602 to 654 when depending directly or indirectly from embodiment 576, wherein the antigen-binding fragment comprises an anti-glyco-LAMP1 variable light chain comprising the amino acid sequence of DVVMTQSPLSLPVTLGQPASISCRSSQSLVHSNGNTYLHWYQQRPQGQSPRLLINKVSNRFSG VPDRFSGSGSGTDFTLKISRVEAEDVGVYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO: 146).

660. The chimeric TCR of any one of embodiments 602 to 654 when depending directly or indirectly from embodiment 576, wherein the antigen-binding fragment comprises an anti-glyco-LAMP1 variable light chain comprising the amino acid sequence of

DVVMTQSPLSLPVTLGQPASISCRSSQSLVHSNANVYLHWFQQRPGQSPRLLINKVSNRFSGV
PDRFSGSGSGTDFTLKISRVEAEDVGVYYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO: 147).

661. The chimeric TCR of any one of embodiments 602 to 654 when depending directly or indirectly from embodiment 576, wherein the antigen-binding fragment comprises an anti-glyco-LAMP1 variable light chain comprising the amino acid sequence of
DVVMTQSPDSLAVSLGERATINCRSSQSLVHSNGNTYLHWYQQKPGQPPKLLINKVSNRFSG
VPDRFSGSGSGTDFTLTISLQAEDVAVYFCSQSTHVPRTFGGGTKVEIK (SEQ ID NO: 148).

662. The chimeric TCR of any one of embodiments 602 to 654 when depending directly or indirectly from embodiment 576, wherein the antigen-binding fragment comprises an anti-glyco-LAMP1 variable light chain comprising the amino acid sequence of
DVVMTQSPDSLAVSLGERATINCKSSQSLHNSNGNTYLHWYQQKPGQPPKLLINKVSTRFSGV
PDRFSGSGSGTDFTLTISLQAEDVAVYYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO: 149).

663. The chimeric TCR of any one of embodiments 602 to 654 when depending directly or indirectly from embodiment 576, wherein the antigen-binding fragment comprises an anti-glyco-LAMP1 variable light chain comprising the amino acid sequence of
DVVMTQSPDSLAVSLGERATINCKSSQSLHNSNANVYLHWYQQKPGQPPKLLINKASTRESGV
PDRFSGSGSGTDFTLTISLQAEDVAVYYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO: 150).

664. The chimeric TCR of any one of embodiments 602 to 654 when depending directly or indirectly from embodiment 576, wherein the antigen-binding fragment comprises an anti-glyco-LAMP1 variable light chain comprising the amino acid sequence of
DVVMTQSPASLAVSPGQRATITCRSSQSLVHSNGNTYLHWYQQKPGQPPKLLINKVSNRFSG
VPAFSGSGSGTDFTLTINPVEANDTANYFCSQSTHVPRTFGGGTKVEIK (SEQ ID NO: 151).

665. The chimeric TCR of any one of embodiments 602 to 654 when depending directly or indirectly from embodiment 576, wherein the antigen-binding fragment comprises an anti-glyco-LAMP1 variable light chain comprising the amino acid sequence of
DVVLTSQSPASLAVSPGQRATITCRSSESLSHSNGNTYLHWYQQKPGQPPKLLINKVSNKFTGV
PARFSGSGSGTDFTLTINPVEANDTANYYYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO: 152).

666. The chimeric TCR of any one of embodiments 602 to 654 when depending directly or indirectly from embodiment 576, wherein the antigen-binding fragment comprises an anti-glyco-LAMP1 variable light chain comprising the amino acid sequence of
DVVLTSQSPASLAVSPGQRATITCRASESLSHSNANVYIHWYQQKPGQPPKLLINKASNKFTGV
PARFSGSGSGTDFTLTINPVEANDTANYYYCSQSTHVPRTFGGGTKVEIK (SEQ ID NO: 153).

667. The chimeric TCR of any one of embodiments 602 to 654, when depending directly or indirectly from embodiment 576, wherein the antigen-binding fragment comprises an anti-glyco-LAMP1 variable light chain comprising:

- (a) a CDR-L1 comprising the amino acid sequence of QSLVHX₆NGNTY (SEQ ID NO:70), or RSSQSLVHX₆NGNTYLH (SEQ ID NO:76),

- (b) a CDR-L2 comprising the amino acid sequence of KVS (SEQ ID NO:71), or KVSX₇RFX₈ (SEQ ID NO:77); and
- (c) a CDR-L3 comprising the amino acid sequence of SQSTHVPRT (SEQ ID NO:72).

668. The chimeric TCR of any one of embodiments 607, 608, 614 to 616, 620, and 621, when comprising a first and/or a second linker, the first and/or second linkers comprise, individually, a constant domain or fragment thereof from an immunoglobulin or from a T cell receptor subunit.

669. The chimeric TCR of embodiment 668, wherein the first and/or second linkers comprise, individually, a CH1, CH2, CH3, CH4, or CL antibody domain, or a fragment of any one thereof.

670. The chimeric TCR of embodiment 668, wherein the first and/or second linkers comprise, individually, a C α , C β , C γ , or C δ TCR domain, or a fragment of any one thereof.

671. The chimeric TCR of embodiment 670, wherein the first polypeptide chain comprises a C α TCR domain or a fragment thereof, and the second polypeptide chain comprises a C β TCR domain or a fragment thereon.

672. The chimeric TCR of embodiment 670, wherein the first polypeptide chain comprises a C β TCR domain or a fragment thereof, and the second polypeptide chain comprises a C α TCR domain or a fragment thereon.

673. The chimeric TCR of embodiment 670, wherein the first polypeptide chain comprises a C γ TCR domain or a fragment thereof, and the second polypeptide chain comprises a C δ TCR domain or a fragment thereon.

674. The chimeric TCR of embodiment 670, wherein the first polypeptide chain comprises a C δ TCR domain or a fragment thereof, and the second polypeptide chain comprises a C γ TCR domain or a fragment thereon.

675. The chimeric TCR of any one of embodiments 670 to 674, wherein the first TCR constant region domain and the second TCR constant region domain each comprise at least one mutation relative to the wildtype TCR constant region domain.

676. The chimeric TCR of embodiment 675, wherein the C α TCR domain comprises a substitution at an amino acid corresponding to amino acid position 48 of wildtype human C α TCR and the C β TCR domain comprises a substitution at an amino acid corresponding amino acid position 57 of wildtype human C β TCR.

677. The chimeric TCR of embodiment 675 or 676 wherein the C α TCR domain comprises a substitution at an amino acid corresponding to amino acid position 85 of wildtype human C α TCR and the C β TCR domain comprises a substitution at an amino acid corresponding to amino acid position 88 of wildtype human C β TCR.

678. The chimeric TCR of any one of embodiments 602 to 677, wherein the first TCR domain further comprises a first connecting peptide of a TCR subunit, or a fragment thereof, N-terminal to the first TCR transmembrane domain.

679. The chimeric TCR of any one of embodiments 602 to 678, wherein the second TCR domain further comprises a second connecting peptide of a TCR subunit, or a fragment thereof, N-terminal to the second TCR transmembrane domain.

680. The chimeric TCR of embodiment 679, comprising a disulfide bond between a residue in the first connecting peptide and a residue in the second connecting peptide.

681. The chimeric TCR of any one of embodiments 602 to 680, wherein the first TCR domain further comprises a first TCR intracellular domain comprising a TCR intracellular sequence C-terminal to the first transmembrane domain.

682. The chimeric TCR of any one of embodiments 602 to 681, wherein the second TCR domain further comprises a second TCR intracellular domain comprising a TCR intracellular sequence C-terminal to the second transmembrane domain.

683. The chimeric TCR of any one of embodiments 602 to 682, wherein the first polypeptide chain further comprises a first accessory intracellular domain comprising a co-stimulatory intracellular signaling sequence C-terminal to the first transmembrane domain.

684. The chimeric TCR of any one of embodiments 602 to 683, wherein the second polypeptide chain further comprises a second accessory intracellular domain comprising a co-stimulatory intracellular signaling sequence C-terminal to the second transmembrane domain.

685. The chimeric TCR of any one of embodiments 602 to 684, further comprising a cleavable peptide linker, configured to temporarily associate the first polypeptide chain with the second polypeptide chain during and/or shortly after protein translation.

686. The chimeric TCR of embodiment 685, wherein the cleavable peptide linker is a protease cleavable peptide linker.

687. The chimeric TCR of embodiment 685 or 686, wherein the peptide linker comprises the sequence ATNFSLLKQAGDVEENPGP (SEQ ID NO: 184).

688. The chimeric TCR of any one of embodiments 602 to 687, wherein the first TCR domain is a TCR α chain or a fragment thereof and the second TCR domain is a TCR β chain or a fragment thereof.

689. The chimeric TCR of any one of embodiments 602 to 687, wherein the first TCR domain is a TCR β chain or a fragment thereof and the second TCR domain is a TCR α chain or a fragment thereof.

690. The chimeric TCR of any one of embodiments 602 to 687, wherein the first TCR domain is a TCR δ chain or a fragment thereof and the second TCR domain is a TCR γ chain or a fragment thereof.

691. The chimeric TCR of any one of embodiments 602 to 687, wherein the first TCR domain is a TCR γ chain or a fragment thereof and the second TCR domain is a TCR δ chain or a fragment thereof.

692. The chimeric TCR of any one of embodiments 602 to 691, comprising, from N- to C-terminus, (i) the anti-glyco-LAMP1 variable heavy chain (VH), (ii) the first TCR domain, (iii) a cleavable peptide linker, (iv) the anti-glyco-LAMP1 variable light chain (VL), and (v) the second TCR domain.

693. The chimeric TCR of any one of embodiments 602 to 691, comprising, from N- to C-terminus, (i) the anti-glyco-LAMP1 variable heavy chain (VH), (ii) the second TCR domain, (iii) a cleavable peptide linker, (iv) the anti-glyco-LAMP1 common light chain (CL), and (v) first second TCR domain.

694. The chimeric TCR of any one of embodiments 602 to 691, comprising, from N- to C-terminus, (i) the anti-glyco-LAMP1 variable light chain (VL), (ii) the first TCR domain, (iii) a cleavable peptide linker, (iv) the anti-glyco-LAMP1 variable heavy chain (VH), and (v) the second TCR domain.

695. The chimeric TCR of any one of embodiments 602 to 691, comprising, from N- to C-terminus, (i) the anti-glyco-LAMP1 variable light chain (VL), (ii) the second TCR domain, (iii) a cleavable peptide linker, (iv) the anti-glyco-LAMP1 variable heavy chain (VH), and (v) the first TCR domain.

696. A nucleic acid comprising a coding region for an anti-glyco-LAMP1 antibody or antigen-binding fragment of any of embodiments 1 to 526, the bispecific antibody of any one of embodiments 527 to 532, the fusion protein of any one of embodiments 533 to 557, the CAR of any one of embodiments 558 to 591, or the chimeric TCR of any one of embodiments 602 to 695.

697. The nucleic acid of embodiment 696 in which the coding region is codon-optimized for expression in a human cell.

698. A vector comprising the nucleic acid of embodiment 696 or embodiment 697.

699. The vector of embodiment 698 which is a viral vector.

700. The vector of embodiment 699 wherein the viral vector is a lentiviral vector.

701. A host cell engineered to express the nucleic acid of embodiment 696 or embodiment 697.

702. The host cell of embodiment 701, which is a human T-cell engineered to express the CAR of any one of embodiments 558 to 591.

703. The host cell of embodiment 701, which is a human NK cell engineered to express the CAR of any one of embodiments 558 to 591.

704. The host cell of embodiment 701, which is a human T-cell engineered to express the chimeric TCR of any one of embodiments 602 to 695.

705. A host cell comprising the vector of any one of embodiments 698 to 700.

706. The host cell of embodiment 705 which is a T-cell and wherein the vector encodes the CAR of any one of embodiments 559 to 592.

707. The host cell of embodiment 705 which is a T-cell and wherein the vector encodes the chimeric TCR of any one of embodiments 602 to 695.

708. A pharmaceutical composition comprising (a) the anti-glyco-LAMP1 antibody or antigen binding fragment of any of embodiments 1 to 526, the bispecific antibody of any one of embodiments 527 to 532, the fusion protein of any one of embodiments 533 to 557, the CAR of any one of embodiments 558 to 591, the antibody-drug conjugate of any one of embodiments 592 to 601, the chimeric TCR of any one of embodiments 602 to 695, the nucleic acid of embodiment 696 or embodiment 697, the vector of any one of embodiments 698 to 700, or the host cell of any one of embodiments 701 to 707, and (b) a physiologically suitable buffer, adjuvant, diluent, or combination thereof.

709. A method of treating cancer comprising administering to a subject in need thereof an effective amount of the anti-glyco-LAMP1 antibody or antigen binding fragment of any of embodiments 1 to 526, the bispecific antibody of any one of embodiments 527 to 532, the fusion protein of any one of embodiments 533 to 557, the CAR of any one of embodiments 558 to 591, the antibody-drug conjugate of any one of embodiments 592 to 601, the chimeric TCR of any one of embodiments 602 to 695, the nucleic acid of embodiment 696 or embodiment 697, the vector of any one of embodiments 698 to 700, the host cell of any one of embodiments 701 to 707, or the pharmaceutical composition of embodiment 708.

710. The method of embodiment 709, wherein the subject is suffering from colorectal neoplasm, colon adenocarcinoma, pancreatic adenocarcinoma, breast adenocarcinoma, or non-small cell lung cancer.

711. The method of embodiment 710, wherein the subject is suffering from colorectal neoplasm.

712. The method of embodiment 710, wherein the subject is suffering from colon adenocarcinoma.

713. The method of embodiment 710, wherein the subject is suffering from pancreatic adenocarcinoma.

714. The method of embodiment 710, wherein the subject is suffering from breast adenocarcinoma.

715. The method of embodiment 710, wherein the subject is suffering from non-small cell lung cancer.

716. A method of detecting cancer in a biological sample, comprising contacting a sample (e.g., a sample comprising or suspected of comprising cancer cells and/or cancer-derived extracellular vesicles) with an anti-glyco-LAMP1 antibody or antigen-binding fragment according to any one of embodiments 1 to 526 and detecting binding of the anti-glyco-LAMP1 antibody or antigen-binding fragment.

717. The method of embodiment 716, further comprising quantitating the binding of the anti-glyco-LAMP1 antibody or antigen-binding fragment.

718. The method of embodiment 716 or embodiment 717, wherein the binding is compared to a normal tissue control as a negative/baseline control and/or to a cancerous tissue control as a positive control.

719. The method of any one of embodiments 716 to 718, wherein the cancer is colorectal neoplasm, colon adenocarcinoma, pancreatic adenocarcinoma, breast adenocarcinoma, or non-small cell lung cancer.

720. The method of embodiment 719, wherein the cancer is colorectal neoplasm.

721. The method of embodiment 719, wherein the cancer is colon adenocarcinoma.

722. The method of embodiment 719, wherein the cancer is pancreatic adenocarcinoma.

723. The method of embodiment 719, wherein the cancer is breast adenocarcinoma.

724. The method of embodiment 719, wherein the cancer is non-small cell lung cancer.

725. The method of any one of embodiments 709 to 724, when depending from any one of embodiments 539 to 542, which further comprises administering to the subject genetically modified T-cells engineered to express a CAR comprising a NKG2D receptor capable of specifically binding the MIC protein domain.

726. The anti-glyco-LAMP1 antibody or antigen binding fragment of any of embodiments 1 to 526, the bispecific antibody of any one of embodiments 527 to 532, the fusion protein of any one of embodiments 533 to 557, the CAR of any one of embodiments 558 to 591, the antibody-drug conjugate of any one of embodiments 592 to 601, the chimeric TCR of any one of embodiments 602 to 695, the nucleic acid of embodiment 696 or embodiment 697, the vector of any one of embodiments 698 to 700, the host cell of any one of embodiments 701 to 707, or the pharmaceutical composition of embodiment 708 for use as a medicament.

727. The anti-glyco-LAMP1 antibody or antigen binding fragment of any of embodiments 1 to 526, the bispecific antibody of any one of embodiments 527 to 532, the fusion protein of any one of embodiments 533 to 557, the CAR of any one of embodiments 558 to 591, the antibody-drug conjugate of any one of embodiments 592 to 601, the chimeric TCR of any one of embodiments 602 to 695, the nucleic acid of embodiment 696 or embodiment 697, the vector of any one of embodiments 698 to 700, the host cell of any one of embodiments 701 to 707, or the pharmaceutical composition of embodiment 708 for use in the treatment of cancer, optionally wherein the cancer is colorectal neoplasm, colon adenocarcinoma, pancreatic adenocarcinoma, breast adenocarcinoma, or non-small cell lung cancer.

728. The anti-glyco-LAMP1 antibody or antigen binding fragment of any of embodiments 1 to 526, the bispecific antibody of any one of embodiments 527 to 532, the fusion protein of any one of embodiments 533 to 557, the CAR of any one of embodiments 558

to 591, the antibody-drug conjugate of any one of embodiments 592 to 601, the chimeric TCR of any one of embodiments 602 to 695, the nucleic acid of embodiment 696 or embodiment 697, the vector of any one of embodiments 698 to 700, the host cell of any one of embodiments 701 to 707, or the pharmaceutical composition of embodiment 708 for use in the treatment of colorectal neoplasm.

729. The anti-glyco-LAMP1 antibody or antigen binding fragment of any of embodiments 1 to 526, the bispecific antibody of any one of embodiments 527 to 532, the fusion protein of any one of embodiments 533 to 557, the CAR of any one of embodiments 558 to 591, the antibody-drug conjugate of any one of embodiments 592 to 601, the chimeric TCR of any one of embodiments 602 to 695, the nucleic acid of embodiment 696 or embodiment 697, the vector of any one of embodiments 698 to 700, the host cell of any one of embodiments 701 to 707, or the pharmaceutical composition of embodiment 708 for use in the treatment of colon adenocarcinoma.

730. The anti-glyco-LAMP1 antibody or antigen binding fragment of any of embodiments 1 to 526, the bispecific antibody of any one of embodiments 527 to 532, the fusion protein of any one of embodiments 533 to 557, the CAR of any one of embodiments 558 to 591, the antibody-drug conjugate of any one of embodiments 592 to 601, the chimeric TCR of any one of embodiments 602 to 695, the nucleic acid of embodiment 696 or embodiment 697, the vector of any one of embodiments 698 to 700, the host cell of any one of embodiments 701 to 707, or the pharmaceutical composition of embodiment 708 for use in the treatment of pancreatic adenocarcinoma.

731. The anti-glyco-LAMP1 antibody or antigen binding fragment of any of embodiments 1 to 526, the bispecific antibody of any one of embodiments 527 to 532, the fusion protein of any one of embodiments 533 to 557, the CAR of any one of embodiments 558 to 591, the antibody-drug conjugate of any one of embodiments 592 to 601, the chimeric TCR of any one of embodiments 602 to 695, the nucleic acid of embodiment 696 or embodiment 697, the vector of any one of embodiments 698 to 700, the host cell of any one of embodiments 701 to 707, or the pharmaceutical composition of embodiment 708 for use in the treatment of breast adenocarcinoma.

732. The anti-glyco-LAMP1 antibody or antigen binding fragment of any of embodiments 1 to 526, the bispecific antibody of any one of embodiments 527 to 532, the fusion protein of any one of embodiments 533 to 557, the CAR of any one of embodiments 558 to 591, the antibody-drug conjugate of any one of embodiments 592 to 601, the chimeric TCR of any one of embodiments 602 to 695, the nucleic acid of embodiment 696 or embodiment 697, the vector of any one of embodiments 698 to 700, the host cell of any one of embodiments 701 to 707, or the pharmaceutical composition of embodiment 708 for use in the treatment of non-small cell lung cancer.

733. Use of the anti-glyco-LAMP1 antibody or antigen binding fragment of any of embodiments 1 to 526, the bispecific antibody of any one of embodiments 527 to 532, the fusion protein of any one of embodiments 533 to 557, the CAR of any one of embodiments 558 to 591, the antibody-drug conjugate of any one of embodiments 592 to 601, the chimeric TCR of any one of embodiments 602 to 695, the nucleic acid of embodiment 696 or embodiment 697, the vector of any one of embodiments 698 to 700, the host cell of any one of embodiments 701 to 707, or the pharmaceutical composition of embodiment 708 for the manufacture of a medicament for the treatment of cancer, optionally wherein the cancer is colorectal neoplasm, colon adenocarcinoma, pancreatic adenocarcinoma, breast adenocarcinoma, or non-small cell lung cancer.

734. The use according to embodiment 733, wherein the cancer is colorectal neoplasm.

735. The use according to embodiment 733, wherein the cancer is colon adenocarcinoma.

736. The use according to embodiment 733, wherein the cancer is pancreatic adenocarcinoma.

737. The use according to embodiment 733, wherein the cancer is breast adenocarcinoma.

738. The use according to embodiment 733, wherein the cancer is non-small cell lung cancer.

739. A peptide of 13-30 amino acids in length comprising a LAMP1 peptide comprising CEQDRPSPTTAPPAPPSPSP (SEQ ID NO:155) or a fragment thereof comprising amino acids corresponding to amino acids 7-10 of CEQDRPSPTTAPPAPPSPSP (SEQ ID NO:155).

740. The peptide of embodiment 739 which is 15-25 amino acids in length.

741. The peptide of embodiment 739 which is 18-25 amino acids in length.

742. The peptide of any one of embodiments 739 to 741, wherein the fragment of the LAMP1 peptide comprises amino acids 5-11, 5-12, 5-13, 5-14, 5-15, 5-16, 5-17, 5-18, 5-19, or 5-20 of SEQ ID NO:155.

743. The peptide of any one of embodiments 739 to 741, wherein the fragment of the LAMP1 peptide comprises amino acids 4-11, 4-12, 4-13, 4-14, 4-15, 4-16, 4-17, 4-18, 4-19, or 4-20 of SEQ ID NO:155.

744. The peptide of any one of embodiments 739 to 741, wherein the fragment of the LAMP1 peptide comprises amino acids 3-11, 3-12, 3-13, 3-14, 3-15, 3-16, 3-17, 3-18, 3-19, or 3-20 of SEQ ID NO:155.

745. The peptide of any one of embodiments 739 to 741, wherein the fragment of the LAMP1 peptide comprises amino acids 2-11, 2-12, 2-13, 2-14, 2-15, 2-16, 2-17, 2-18, 2-19, or 2-20 of SEQ ID NO:155.

746. The peptide of any one of embodiments 739 to 741, wherein the fragment of the LAMP1 peptide comprises amino acids 1-11, 1-12, 1-13, 1-14, 1-15, 1-16, 1-17, 1-18, 1-19, or 1-20 of SEQ ID NO:155.

747. The peptide of any one of embodiments 739 to 741 which comprises CEQDRPSPTTAPPAPPSPSP (SEQ ID NO:155).

748. The peptide of any one of embodiments 739 to 741 which consists of CEQDRPSPTTAPPAPPSPSP (SEQ ID NO:155).

749. The peptide of any one of embodiments 739 to 748 which is O-glycosylated at:

- (a) the threonine corresponding to position 9 of CEQDRPSPTTAPPAPPSPSP (SEQ ID NO:155);
- (b) the threonine corresponding to position 9 of CEQDRPSPTTAPPAPPSPSP (SEQ ID NO:155) and the threonine corresponding to position 10 of CEQDRPSPTTAPPAPPSPSP (SEQ ID NO:155);
- (c) the threonine corresponding to position 9 of CEQDRPSPTTAPPAPPSPSP (SEQ ID NO:155) and the serine corresponding to position 7 of CEQDRPSPTTAPPAPPSPSP (SEQ ID NO:155); or
- (d) the serine corresponding to position 7 of CEQDRPSPTTAPPAPPSPSP (SEQ ID NO:155), the threonine corresponding to position 9 of CEQDRPSPTTAPPAPPSPSP (SEQ ID NO:155) and the threonine corresponding to position 10 of CEQDRPSPTTAPPAPPSPSP (SEQ ID NO:155).

750. The peptide of embodiment 749, wherein the O-glycosylation comprises or consists of GalNAc.

751. A peptide of 13-30 amino acids in length comprising amino acids amino acids 5-11 of a LAMP1 peptide CEQDRPS**IT**APPAPPSPSP (SEQ ID NO:200) that has been O-glycosylated on the threonine residue shown with bold and underlined text.

752. A peptide of 13-30 amino acids in length comprising amino acids amino acids 5-11 of a LAMP1 peptide CEQDRPS**TT**APPAPPSPSP (SEQ ID NO:216) that has been O-glycosylated on the threonine residues shown with bold and underlined text.

753. A peptide of 13-30 amino acids in length comprising amino acids amino acids 5-11 of a LAMP1 peptide CEQDRP**SP****IT**APPAPPSPSP (SEQ ID NO:217) that has been O-glycosylated on the serine and threonine residues shown with bold and underlined text.

754. A peptide of 13-30 amino acids in length comprising amino acids amino acids 5-11 of a LAMP1 peptide CEQDRP**SP****TT**APPAPPSPSP (SEQ ID NO:154) that has been O-glycosylated on the serine and threonine residues shown with bold and underlined text.

755. The peptide of any one of embodiments 751 to 754 which is 15-25 amino acids in length.

756. The peptide of any one of embodiments 751 to 755 which is 18-25 amino acids in length.

757. The peptide of embodiment 751 which comprises CEQDRPSPITAPPAPPSPSP (SEQ ID NO:200).

758. The peptide of embodiment 751 which consists of CEQDRPSPITAPPAPPSPSP (SEQ ID NO:200).

759. The peptide of embodiment 752 which comprises CEQDRPSPITAPPAPPSPSP (SEQ ID NO:216).

760. The peptide of embodiment 752 which consists of CEQDRPSPITAPPAPPSPSP (SEQ ID NO:216).

761. The peptide of embodiment 753 which comprises CEQDRPSPITAPPAPPSPSP (SEQ ID NO:217).

762. The peptide of embodiment 753 which consists of CEQDRPSPITAPPAPPSPSP (SEQ ID NO:217).

763. The peptide of embodiment 754 which comprises CEQDRPSPITAPPAPPSPSP (SEQ ID NO:154).

764. The peptide of embodiment 754 which consists of CEQDRPSPITAPPAPPSPSP (SEQ ID NO:154).

765. The peptide of any one of embodiments 751 to 764, wherein the O-glycosylation comprises or consists of GalNAc.

766. A composition comprising the peptide of any one of embodiments 739 to 765 and adjuvant.

767. The composition of embodiment 766, wherein the adjuvant comprises a Freund's adjuvant and/or an aluminum salt (e.g., aluminum hydroxide).

768. A method of generating antibodies against a tumor-associated form of LAMP1, comprising administering to an animal:

- (a) the peptide of any one of embodiments 749 to 765; or
- (b) The composition of embodiment 766 or 767 wherein the composition comprises the peptide of any one of embodiments 749 to 765.

769. The method of embodiment 768, further comprising collecting antibodies from the animal following the administering step.

770. A method of eliciting an immune response against a tumor-associated form of LAMP1, comprising administering to a subject:

- (a) the peptide of any one of embodiments 749 to 765; or
- (b) the composition of embodiment 766 or 767 wherein the composition comprises the peptide of any one of embodiments 749 to 765.

771. The method of any one of embodiments 768 to 770, wherein the animal is a mouse or a rabbit.

772. The anti-glyco-LAMP1 antibody or antigen binding fragment, bispecific antibody, fusion protein, CAR, antibody-drug conjugate, the chimeric TCR, pharmaceutical composition method or use as described in any one of the preceding embodiments, wherein the determination of competing is made using an antibody competition assay, optionally wherein the assay is an assay described in Section 5.1.

773. The anti-glyco-LAMP1 antibody or antigen binding fragment, bispecific antibody, fusion protein, CAR, antibody-drug conjugate, the chimeric TCR, pharmaceutical composition method or use of embodiment 772, wherein competing is present if the anti-glyco-LAMP1 antibody or anti-glyco-LAMP1 antibody fragment decreases binding of a reference antibody by at least about 20% 30%, 40%, 50%, 60%, 70%, 80%, 90%, or 95% when tested at a reference antibody concentration that is 80% of maximal binding under the specific assay conditions used and a test antibody concentration that is 10-fold higher than the reference antibody concentration.

[0451] All publications, patents, patent applications and other documents cited in this application are hereby incorporated by reference in their entireties for all purposes to the same extent as if each individual publication, patent, patent application or other document were individually indicated to be incorporated by reference for all purposes. In the event that there is an inconsistency between the teachings of one or more of the references incorporated herein and the present disclosure, the teachings of the present specification are intended.

What is claimed is:

1. An anti-glyco-LAMP1 antibody or antigen binding fragment that specifically binds to, or specifically competes for binding to:
 - (a) a LAMP1 peptide comprising CEQDRPSP**IT**APPAPPSPSP (SEQ ID NO:200) or a fragment thereof that has been glycosylated with GalNAc on the threonine residue shown with bold and underlined text ("the first LAMP1 glycopeptide");
 - (b) a LAMP1 peptide comprising CEQDRPSP**TT**APPAPPSPSP (SEQ ID NO:216) or a fragment thereof that has been glycosylated with GalNAc on the threonine residues shown with bold and underlined text ("the second LAMP1 glycopeptide");
 - (c) a LAMP1 peptide comprising CEQDRP**SP****IT**APPAPPSPSP (SEQ ID NO:217) or a fragment thereof that has been glycosylated with GalNAc on the serine and threonine residues shown with bold and underlined text ("the third LAMP1 glycopeptide"); or
 - (d) a LAMP1 peptide comprising CEQDRP**SP****TT**APPAPPSPSP (SEQ ID NO:154) or a fragment thereof that has been glycosylated with GalNAc on the serine and threonine residues shown with bold and underlined text ("the fourth LAMP1 glycopeptide").
2. The anti-glyco-LAMP1 antibody or antigen binding fragment of claim 1, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence and a light chain variable (VL) sequence of:
 - (a) SEQ ID NO:1 and SEQ ID NO:2, respectively;
 - (b) SEQ ID NO:23 and SEQ ID NO:24, respectively; or
 - (c) SEQ ID NO:45 and SEQ ID NO:46, respectively.
3. The anti-glyco-LAMP1 antibody or antigen binding fragment of claim 1, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of any one of SEQ ID NOS:133-144 and a light chain variable (VL) sequence of any one of SEQ ID NOS:145-153 for binding to any one of the LAMP1 glycopeptides.
4. The anti-glyco-LAMP1 antibody or antigen binding fragment of any one of claims 1 to 3, which specifically binds to COSMC knock-out T47D cells.
5. The anti-glyco-LAMP1 antibody or antigen binding fragment of claim 4, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence and a light chain variable (VL) sequence of:
 - (a) SEQ ID NO:1 and SEQ ID NO:2, respectively;

(b) SEQ ID NO:23 and SEQ ID NO:24, respectively; or

(c) SEQ ID NO:45 and SEQ ID NO:46, respectively;

for binding to COSMC knock-out T47D cells.

6. The anti-glyco-LAMP1 antibody or antigen binding fragment of claim 4, wherein the anti-glyco-LAMP1 antibody or antigen binding fragment competes with an antibody or antigen binding fragment comprising a heavy chain variable (VH) sequence of any one of SEQ ID NOS:133-144 and a light chain variable (VL) sequence of any one of SEQ ID NOS:145-153 for binding to COSMC knock-out T47D cells.

7. An anti-glyco-LAMP1 antibody or antigen-binding fragment, which is optionally an anti-glyco-LAMP1 antibody or antigen-binding fragment according to any one of claims 1 to 6, comprising:

(a) a complementarity determining region (CDR) H1 comprising the amino acid sequence of SEQ ID NO:67, SEQ ID NO:73, SEQ ID NO:79, SEQ ID NO:103, or SEQ ID NO:127;

(b) a CDR-H2 comprising the amino acid sequence of SEQ ID NO:68, SEQ ID NO:74, SEQ ID NO:80, SEQ ID NO:104, or SEQ ID NO:128;

(c) a CDR-H3 comprising the amino acid sequence of SEQ ID NO:69, SEQ ID NO: 75, SEQ ID NO: 81, SEQ ID NO:105, or SEQ ID NO:129;

(d) a CDR-L1 comprising the amino acid sequence of SEQ ID NO:70, SEQ ID NO:76, SEQ ID NO:82, SEQ ID NO:106, or SEQ ID NO:130;

(e) a CDR-L2 comprising the amino acid sequence of SEQ ID NO:71, SEQ ID NO:77, SEQ ID NO:83, SEQ ID NO:107, or SEQ ID NO:131; and

(f) a CDR-L3 comprising the amino acid sequence of SEQ ID NO:72, SEQ ID NO:78, SEQ ID NO:84, SEQ ID NO:108, or SEQ ID NO:132.

8. An anti-glyco-LAMP1 antibody or antigen-binding fragment, which is optionally an anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of claims 1 to 6, which comprises:

(a) a VH comprising CDR-H1, CDR-H2, and CDR-H3 having the amino sequences of SEQ ID NOS:3-5, respectively, and a VL comprising CDR-L1, CDR-L2, and CDR-L3 having the amino acid sequences of SEQ ID NOS:6-8, respectively;

(b) a VH comprising CDR-H1, CDR-H2, and CDR-H3 having the amino sequences of SEQ ID NOS:9-11, respectively, and a VL comprising CDR-L1, CDR-L2, and CDR-L3 having the amino acid sequences of SEQ ID NOS:12-14, respectively; or

(c) a VH comprising CDR-H1, CDR-H2, and CDR-H3 having the amino sequences of SEQ ID NOS:15-17, respectively, and a VL comprising CDR-L1, CDR-L2, and CDR-L3 having the amino acid sequences of SEQ ID NOS:18-20, respectively.

9. An anti-glyco-LAMP1 antibody or antigen-binding fragment, which is optionally an anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of claims 1 to 6, which comprises:

- (a) a VH comprising CDR-H1, CDR-H2, and CDR-H3 having the amino sequences of SEQ ID NOS:25-27, respectively, and a VL comprising CDR-L1, CDR-L2, and CDR-L3 having the amino acid sequences of SEQ ID NOS:28-30, respectively;
- (b) a VH comprising CDR-H1, CDR-H2, and CDR-H3 having the amino sequences of SEQ ID NOS:31-33, respectively, and a VL comprising CDR-L1, CDR-L2, and CDR-L3 having the amino acid sequences of SEQ ID NOS:34-36, respectively; or
- (c) a VH comprising CDR-H1, CDR-H2, and CDR-H3 having the amino sequences of SEQ ID NOS:37-39, respectively, and a VL comprising CDR-L1, CDR-L2, and CDR-L3 having the amino acid sequences of SEQ ID NOS:40-42, respectively.

10. An anti-glyco-LAMP1 antibody or antigen-binding fragment, which is optionally an anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of claims 1 to 6, which comprises:

- (a) a VH comprising CDR-H1, CDR-H2, and CDR-H3 having the amino sequences of SEQ ID NOS:47-49, respectively, and a VL comprising CDR-L1, CDR-L2, and CDR-L3 having the amino acid sequences of SEQ ID NOS:50-52, respectively;
- (b) a VH comprising CDR-H1, CDR-H2, and CDR-H3 having the amino sequences of SEQ ID NOS:53-55, respectively, and a VL comprising CDR-L1, CDR-L2, and CDR-L3 having the amino acid sequences of SEQ ID NOS:56-58, respectively; or
- (c) a VH comprising CDR-H1, CDR-H2, and CDR-H3 having the amino sequences of SEQ ID NOS:59-61, respectively, and a VL comprising CDR-L1, CDR-L2, and CDR-L3 having the amino acid sequences of SEQ ID NOS:62-64, respectively.

11. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of claims 1 to 10, which is a chimeric or humanized antibody or antigen-binding fragment of a chimeric or humanized antibody.

12. An anti-glyco-LAMP1 antibody or antigen-binding fragment, which is optionally anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of claims 1 to 11, which comprises:

- (a) a VH comprising an amino acid sequence having at least 95% sequence identity to SEQ ID NO:1 and a VL comprising an amino acid sequence having at least 95% sequence identity to SEQ ID NO:2;
- (b) a VH comprising an amino acid sequence having at least 95% sequence identity to SEQ ID NO:23 and a VL comprising an amino acid sequence having at least 95% sequence identity to SEQ ID NO:24; or

(c) a VH comprising an amino acid sequence having at least 95% sequence identity to SEQ ID NO:45 and a VL comprising an amino acid sequence having at least 95% sequence identity to SEQ ID NO:46.

13. An anti-glyco-LAMP1 antibody or antigen-binding fragment, which is optionally an anti-glyco-LAMP1 antibody or antigen-binding fragment according to any one of claims 1 to 12, that competes with a reference antibody or antigen binding fragment comprising:

- (a) a heavy chain variable (VH) sequence of SEQ ID NO:1 and a light chain variable (VL) sequence of SEQ ID NO:2;
- (b) a heavy chain variable (VH) sequence of SEQ ID NO:23 and a light chain variable (VL) sequence of SEQ ID NO:24;
- (c) a heavy chain variable (VH) sequence of SEQ ID NO:45 and a light chain variable (VL) sequence of SEQ ID NO:46; or
- (d) a humanized heavy chain variable (VH) sequence of any one of SEQ ID NOS:133-144 and a humanized light chain variable (VL) sequence of any one of SEQ ID NOS:145-153,

for binding to:

- (a) a LAMP1 peptide comprising CEQDRPSP**IT**APPAPPSPSP (SEQ ID NO:200) or a fragment thereof that has been glycosylated with GalNAc on the threonine residue shown with bold and underlined text ("the first LAMP1 glycopeptide");
- (b) a LAMP1 peptide comprising CEQDRPSP**TT**APPAPPSPSP (SEQ ID NO:216) or a fragment thereof that has been glycosylated with GalNAc on the threonine residues shown with bold and underlined text ("the second LAMP1 glycopeptide");
- (c) a LAMP1 peptide comprising CEQDRP**SPT**APPAPPSPSP (SEQ ID NO:217) or a fragment thereof that has been glycosylated with GalNAc on the serine and threonine residues shown with bold and underlined text ("the third LAMP1 glycopeptide"); or
- (d) a LAMP1 peptide comprising CEQDRP**SPTT**APPAPPSPSP (SEQ ID NO:154) or a fragment thereof that has been glycosylated with GalNAc on the serine and threonine residues shown with bold and underlined text ("the fourth LAMP1 glycopeptide"), the anti-glyco-LAMP1 antibody or antigen-binding fragment comprising:
 - (i) a VH sequence with first, second and third CDR means within the VH sequence; and
 - (ii) a VL sequence with fourth, fifth and sixth CDR means within the VL sequence,

wherein the first, second, third, fourth, fifth, and sixth CDR means cooperate to effect binding of the anti-glyco-LAMP1 antibody or antigen-binding fragment to the first LAMP1

glycopeptide, the second LAMP1 glycopeptide, the third LAMP1 glycopeptide, or the fourth LAMP1 glycopeptide.

14. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of claims 1 to 13, which preferentially binds to a glyco-LAMP1 epitope that is overexpressed on cancer cells as compared to normal cells.

15. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of claims 1 to 14, which binds to the first, second, third, or fourth LAMP1 glycopeptide with a binding affinity (KD) of 1 nM to 200 nM as measured by surface plasmon resonance or bio-layer interferometry.

16. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of claims 1 to 15, which does not specifically bind to the unglycosylated LAMP1 peptide CEQDRPSPTTAPPAPPSPSP (SEQ ID NO: 155) (the “unglycosylated LAMP1 peptide”).

17. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of claims 1 to 16, which does not specifically bind to the MUC1 tandem repeat (VTSAPDTRPAPGSTAPPAHG)₃ (SEQ ID NO:208) that has been glycosylated in vitro using purified recombinant human glycosyltransferases GalNAc-T1, GalNAc-T2, and GalNAc-T4 (“the first MUC1 glycopeptide”).

18. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of claims 1 to 17, which does not specifically bind to the MUC1 peptide TAPPAHGV**TS**APD**TR**PAPG**ST**APPAHGV**T** (SEQ ID NO:209) that has been glycosylated in vitro with GalNAc on the serine and threonine residues shown with bold and underlined text (the “second MUC1 glycopeptide”).

19. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of claims 1 to 18, which does not specifically bind to the podoplanin peptide ERG**IK**PPL**E**ELSGK (SEQ ID NO:211) that has been glycosylated in vitro with GalNAc on the threonine residue shown with bold and underlined text (the “PDPN glycopeptide”).

20. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of claims 1 to 19, which does not specifically bind to the CD44v6 peptide GYRQ**TP**KEDSH**ST**TGTAAA (SEQ ID NO:212) that has been glycosylated in vitro with GalNAc on the threonine and serine residues shown with bold and underlined text (the “CD44v6 glycopeptide”).

21. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of claims 1 to 20, which does not specifically bind to the MUC4 peptide CTIPSTAMHTR**STA**APIILP (SEQ ID

NO:213) that has been glycosylated in vitro with GalNAc on the serine and threonine residues shown with bold and underlined text (the "MUC4 glycopeptide").

22. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of claims 1 to 21, which does not specifically bind to the cMET peptide PTKSFISGG**ST**ITGVGKNLN (SEQ ID NO:214) that has been glycosylated in vitro with GalNAc on the serine and threonine residues shown with bold and underlined text (the "cMET glycopeptide").

23. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of claims 1 to 22, which is multivalent.

24. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of claims 1 to 23, which is an antigen-binding fragment.

25. The anti-glyco-LAMP1 antibody or antigen-binding fragment of claim 24, wherein the antigen-binding fragment is in the form of a single-chain variable fragment (scFv).

26. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any of claims 1 to 23, which is in the form of a multispecific antibody.

27. The anti-glyco-LAMP1 antibody or antigen-binding fragment of claim 26, wherein the multispecific antibody is a bispecific antibody that binds to a second epitope that is different from the first epitope.

28. The anti-glyco-LAMP1 antibody or antigen-binding fragment of claim 27, wherein the bispecific antibody is a bottle opener, mAb-Fv, mAb-scFv, central-scFv, one-armed central-scFv, or dual scFv format bispecific antibody.

29. The anti-glyco-LAMP1 antibody or antigen-binding fragment of claim 27, wherein the bispecific antibody is a bispecific domain-exchanged antibody (e.g., a CrossMab), a Fab-arm exchange antibody, a bispecific T-cell engager (BiTE), or a dual-affinity retargeting molecule (DART).

30. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of claims 27 to 29, wherein the second epitope is a LAMP1 epitope.

31. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of claims 27 to 29, wherein the second epitope is a LAMP1 epitope that is overexpressed on cancer cells as compared to normal cells.

32. The anti-glyco-LAMP1 antibody or antigen-binding fragment of any one of claims 27 to 29, wherein the second epitope is a T-cell epitope.

33. The anti-glyco-LAMP1 antibody or antigen-binding fragment of claim 33, wherein the T-cell epitope comprises a CD3 epitope, a CD8 epitope, a CD16 epitope, a CD25 epitope, a CD28 epitope, or an NKG2D epitope.

34. A fusion protein comprising the amino acid sequence of the anti-glyco-LAMP1 antibody or antigen-binding fragment of any of claims 1 to 33, operably linked to at least a second amino acid sequence.

35. A chimeric antigen receptor (CAR) comprising one or more antigen-binding fragments according to claim 24 or claim 25.

36. A chimeric antigen receptor (CAR), whose amino acid sequence comprises the amino acid sequence of SEQ ID NO: 205, SEQ ID NO: 206, or SEQ ID NO: 207.

37. An antibody-drug conjugate comprising the anti-glyco-LAMP1 antibody or antigen-binding fragment of any of claims 1 to 33 or the fusion protein of claim 34 conjugated to a cytotoxic agent.

38. A chimeric T cell receptor (TCR) comprising

- (a) an antigen-binding fragment according to claim 24 or claim 25;
- (b) a first polypeptide chain comprising a first TCR domain comprising a first TCR transmembrane domain from a first TCR subunit; and
- (c) a second polypeptide chain comprising a second TCR domain comprising a second TCR transmembrane domain from a second TCR subunit.

39. A nucleic acid comprising a coding region for an anti-glyco-LAMP1 antibody or antigen-binding fragment of any of claims 1 to 33, the fusion protein of claim 34, the CAR of claim 35 or claim 36, or the chimeric TCR of claim 38.

40. A vector comprising the nucleic acid of claim 39.

41. A host cell engineered to express the nucleic acid of claim 39 or comprising the vector of claim 40.

42. A pharmaceutical composition comprising (a) the anti-glyco-LAMP1 antibody or antigen binding fragment of any of claims 1 to 33, the fusion protein of claim 34, the CAR of claim 35 or claim 36, the antibody-drug conjugate of claim 37, the chimeric TCR of claim 38, the nucleic acid of claim 39, the vector of claim 40, or the host cell of claim 41, and (b) a physiologically suitable buffer, adjuvant, diluent, or combination thereof.

43. A method of treating cancer comprising administering to a subject in need thereof an effective amount of the anti-glyco-LAMP1 antibody or antigen binding fragment of any of claims 1 to 33, the fusion protein of claim 34, the CAR of claim 35 or claim 36, the antibody-drug conjugate of claim 37, the chimeric TCR of claim 38, the nucleic acid of claim 39, the vector of claim 40, the host cell of claim 41, or the pharmaceutical composition of claim 42.

44. The method of claim 43, wherein the subject is suffering from colorectal neoplasm, colon adenocarcinoma, pancreatic adenocarcinoma, breast adenocarcinoma, or non-small cell lung cancer.

45. A method of detecting cancer in a biological sample, comprising contacting a sample (e.g., a sample comprising or suspected of comprising cancer cells and/or cancer-derived extracellular vesicles) with an anti-glyco-LAMP1 antibody or antigen-binding fragment according to any one of claims 1 to 33 and detecting binding of the anti-glyco-LAMP1 antibody or antigen-binding fragment.

46. The method of claim 45, wherein the cancer is colorectal neoplasm, colon adenocarcinoma, pancreatic adenocarcinoma, breast adenocarcinoma, or non-small cell lung cancer.

47. A peptide of 13-30 amino acids in length comprising a LAMP1 peptide comprising CEQDRPSPTTAPPAPPSPSP (SEQ ID NO:155) or a fragment thereof comprising amino acids corresponding to amino acids 7-10 of CEQDRPSPTTAPPAPPSPSP (SEQ ID NO:155).

48. A peptide of 13-30 amino acids in length comprising amino acids amino acids 5-11 of a LAMP1 peptide CEQDRP**SP**ITAPPAPPSPSP (SEQ ID NO:200) that has been O-glycosylated on the threonine residue shown with bold and underlined text.

49. A peptide of 13-30 amino acids in length comprising amino acids amino acids 5-11 of a LAMP1 peptide CEQDRP**SP**ITAPPAPPSPSP (SEQ ID NO:216) that has been O-glycosylated on the threonine residues shown with bold and underlined text.

50. A peptide of 13-30 amino acids in length comprising amino acids amino acids 5-11 of a LAMP1 peptide CEQDRP**SP**ITAPPAPPSPSP (SEQ ID NO:217) that has been O-glycosylated on the serine and threonine residues shown with bold and underlined text.

51. A peptide of 13-30 amino acids in length comprising amino acids amino acids 5-11 of a LAMP1 peptide CEQDRP**SP**ITAPPAPPSPSP (SEQ ID NO:154) that has been O-glycosylated on the serine and threonine residues shown with bold and underlined text.

52. A composition comprising the peptide of any one of claim 47 to 51 and adjuvant.
53. A method of generating antibodies against a tumor-associated form of LAMP1, comprising administering to an animal:
- (a) the peptide of any one of claims 48 to 51; or
 - (b) The composition of claim 52, wherein the composition comprises the peptide of any one of claims 48 to 51.
54. A method of eliciting an immune response against a tumor-associated form of LAMP1, comprising administering to a subject:
- (a) the peptide of any one of claims 48 to 51; or
 - (b) the composition of claim 52, wherein the composition comprises the peptide of any one of claims 48 to 51.

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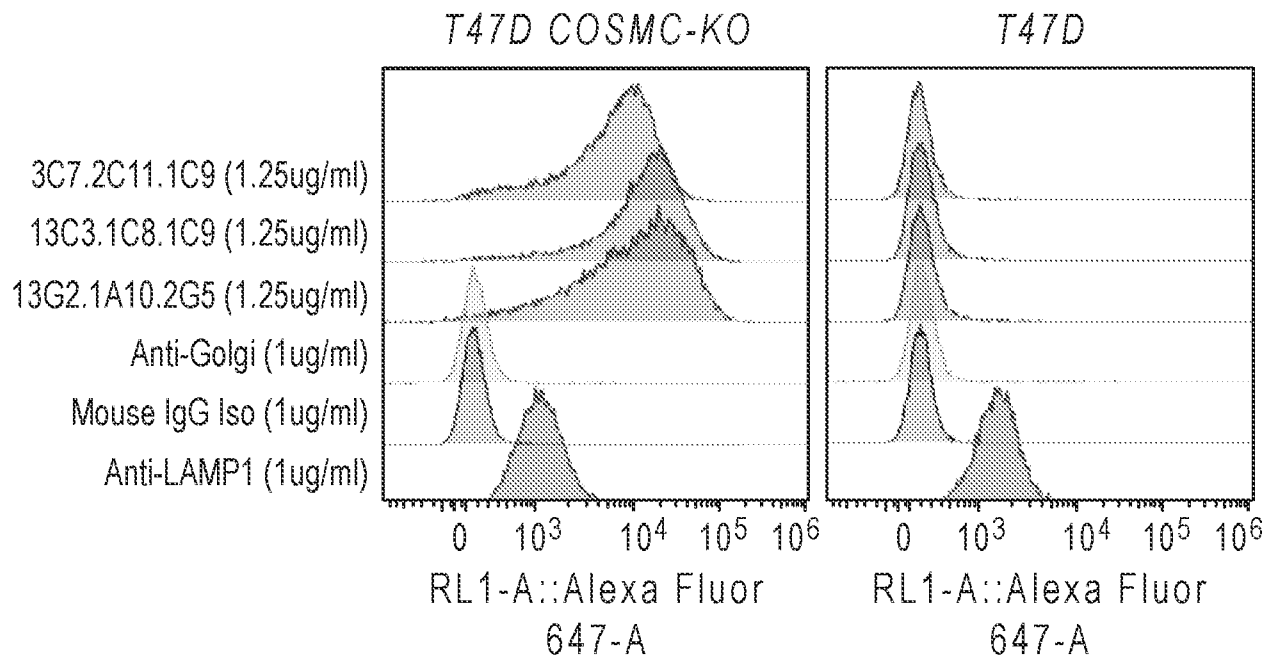


FIG. 1A

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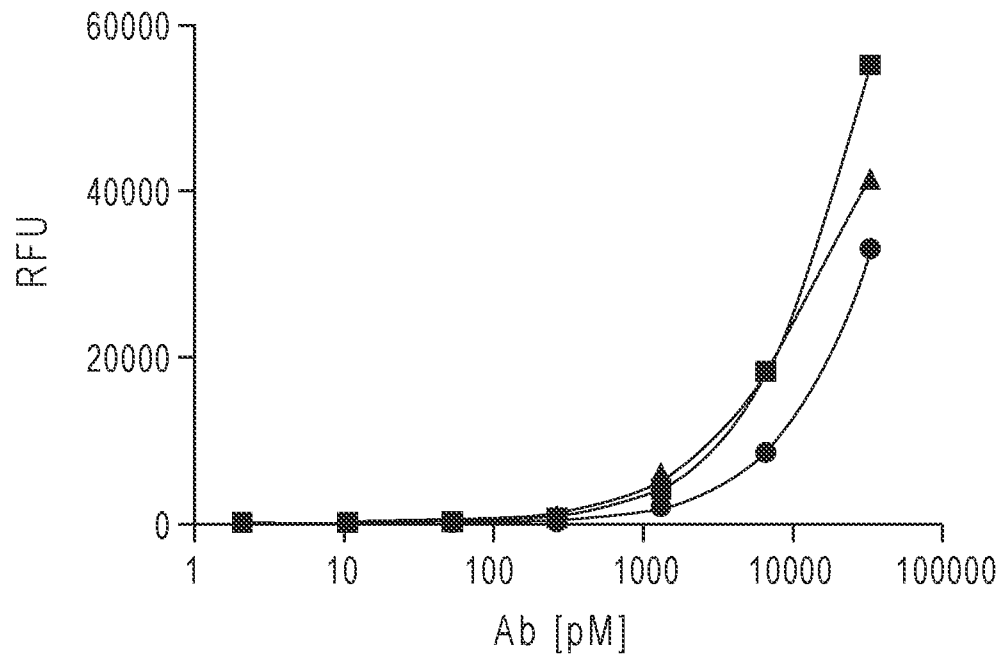
Overlay of Mouse mAbs on T47D COSMC-KO Cells

FIG. 1B-1

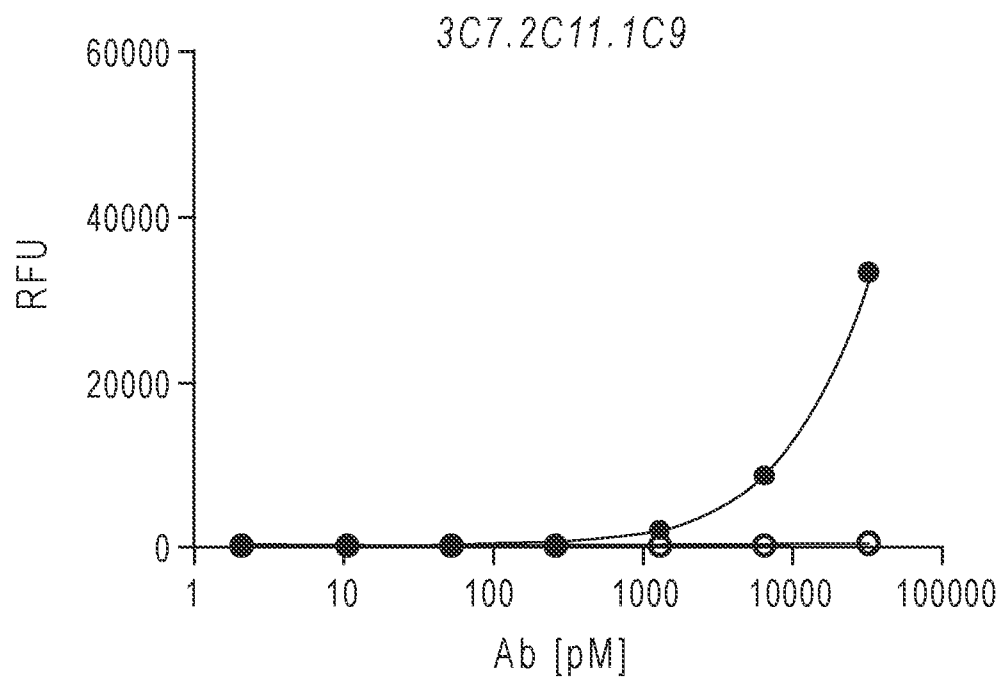


FIG. 1B-2

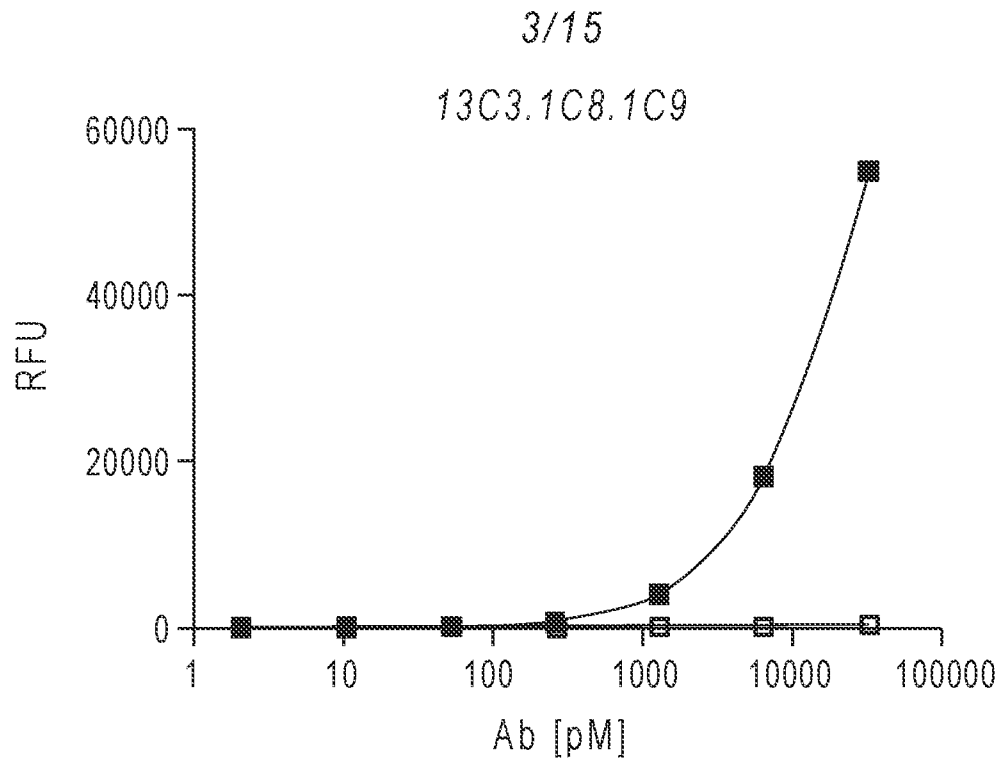


FIG. 1B-3

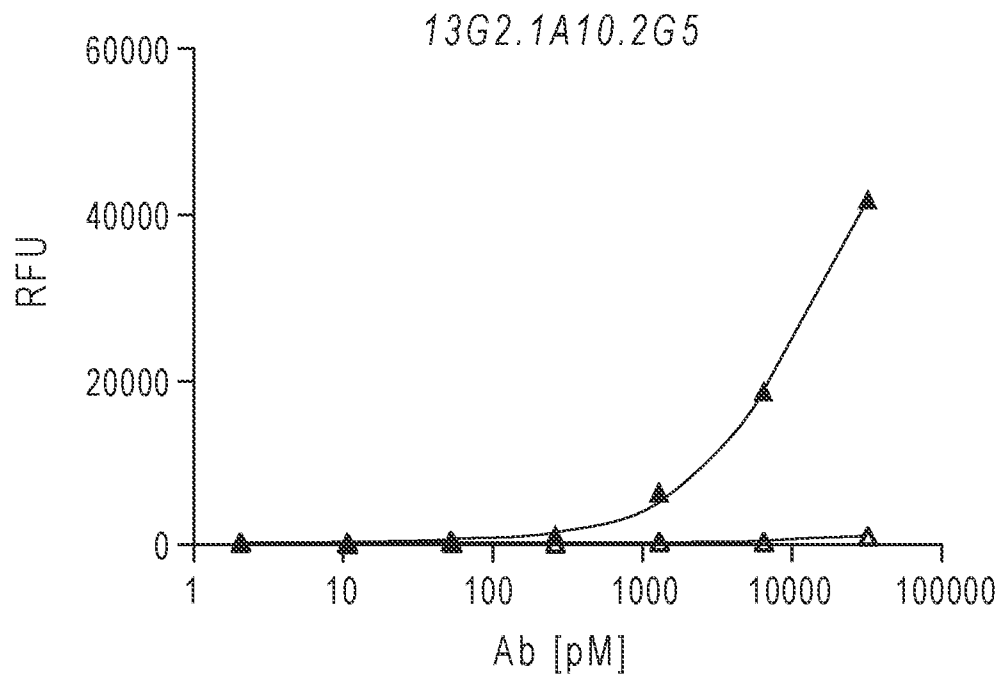


FIG. 1B-4

FIG. 1B-5

Antibody	T47D COSMC-KO	T47D
3C7.2C11.1C9	●	⊙
13C3.1C8.1C9	■	⊠
13G2.1A10.2G5	▲	⬠

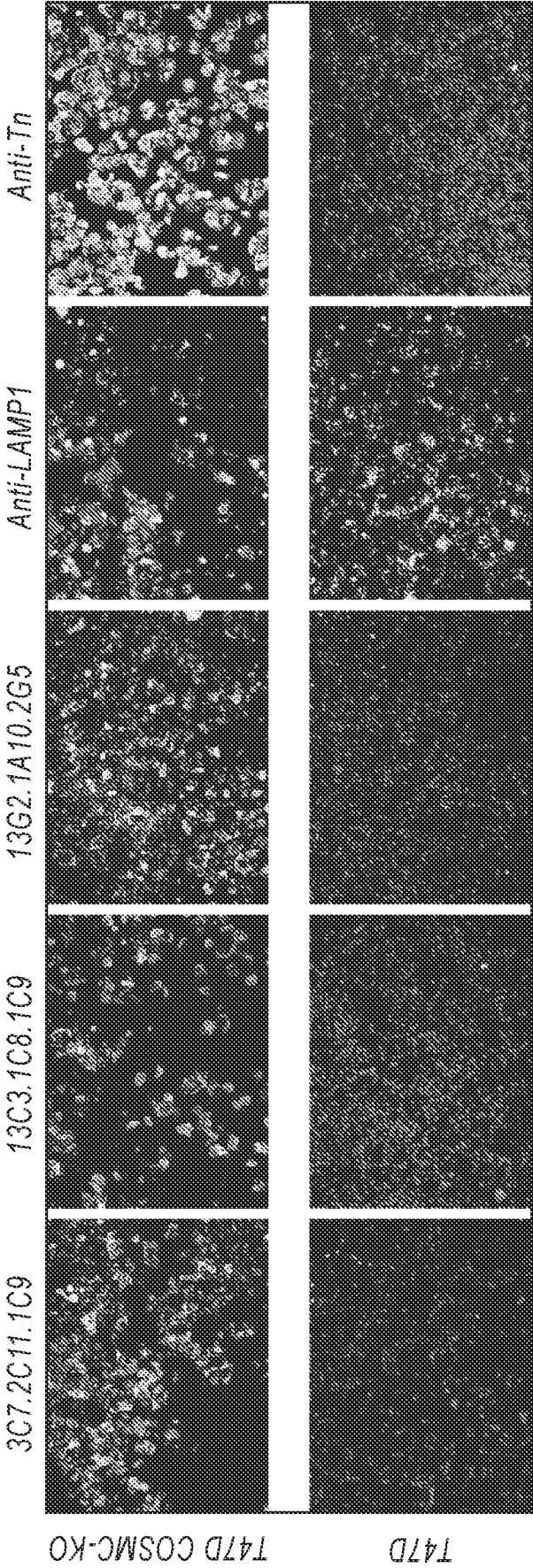


FIG. 2

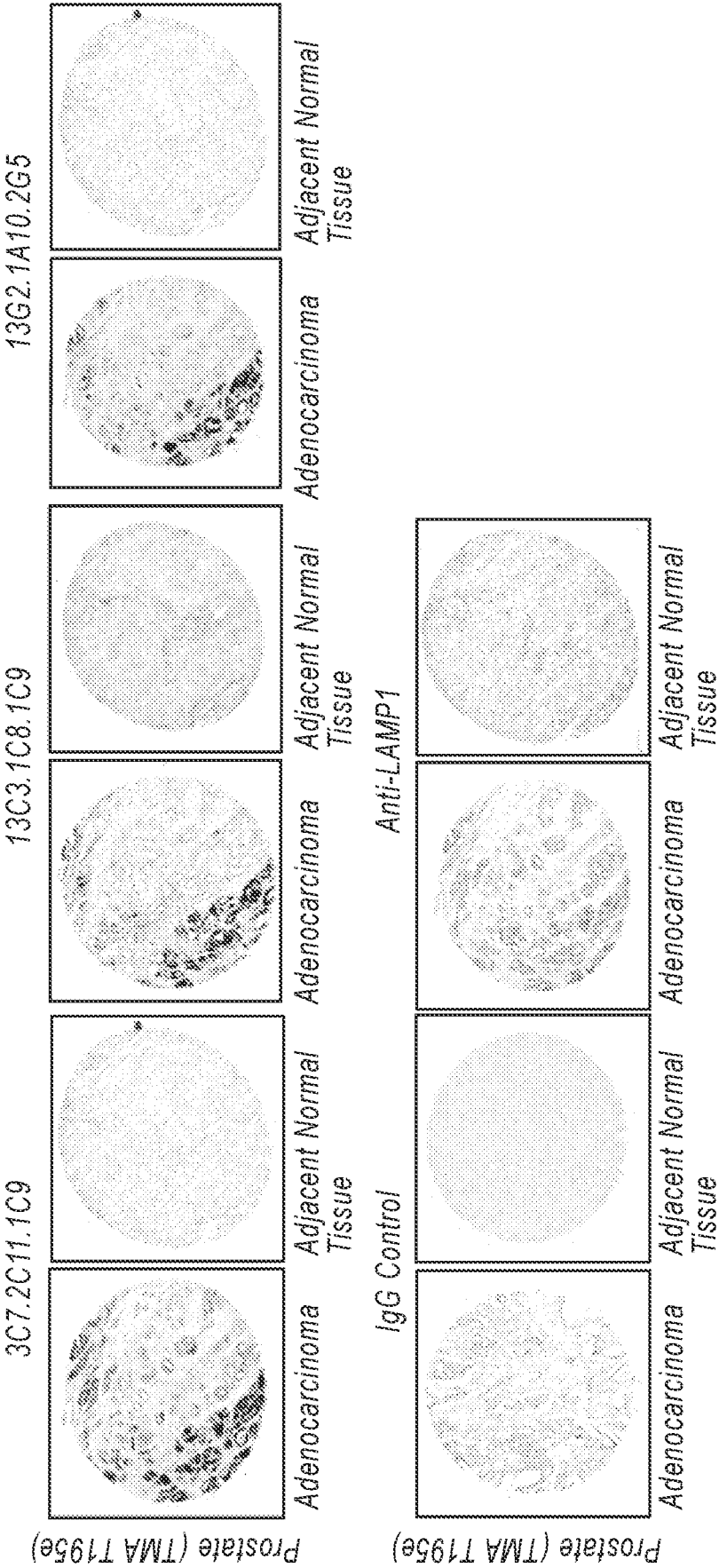


FIG. 3

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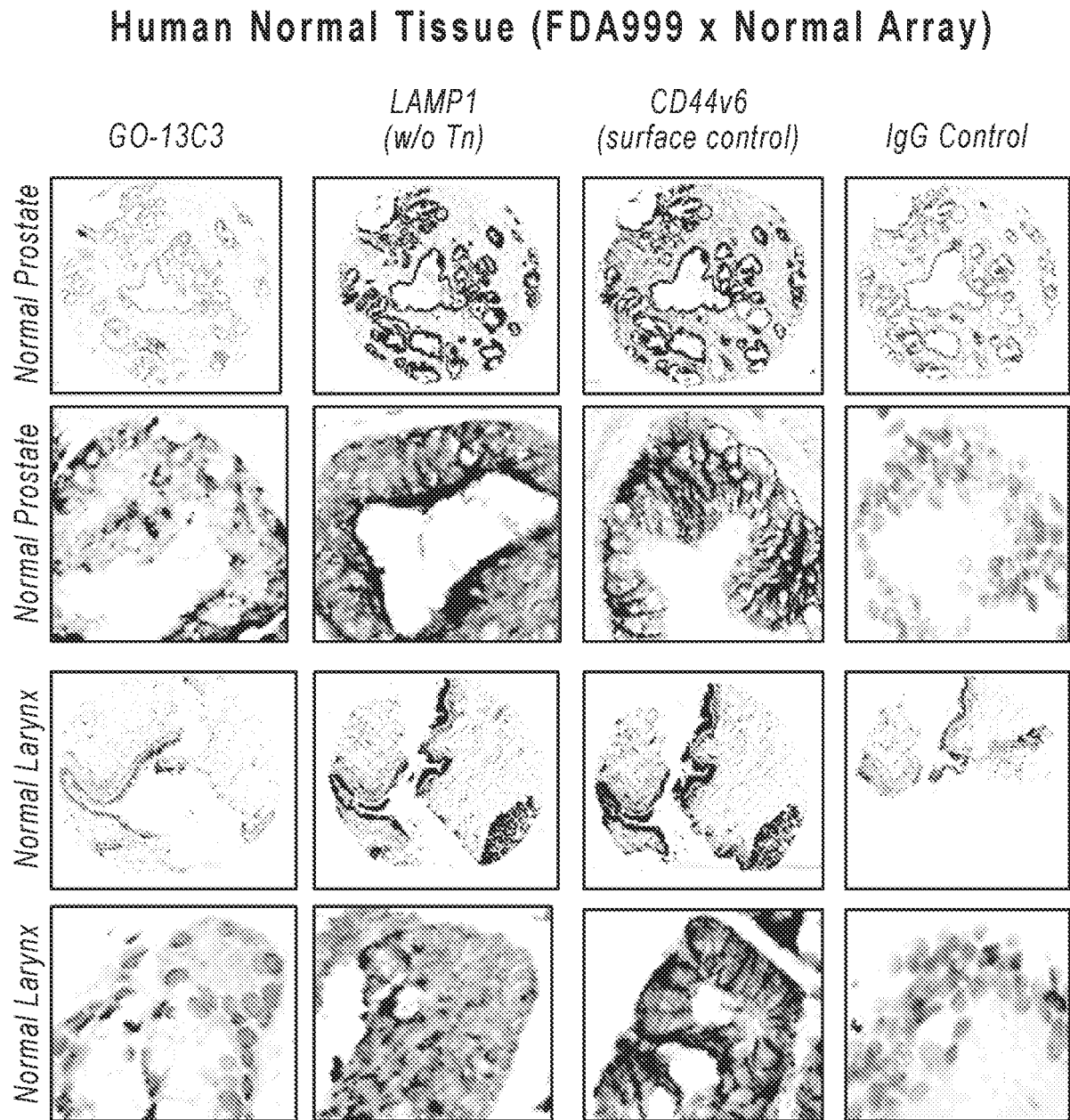


FIG. 4A-1

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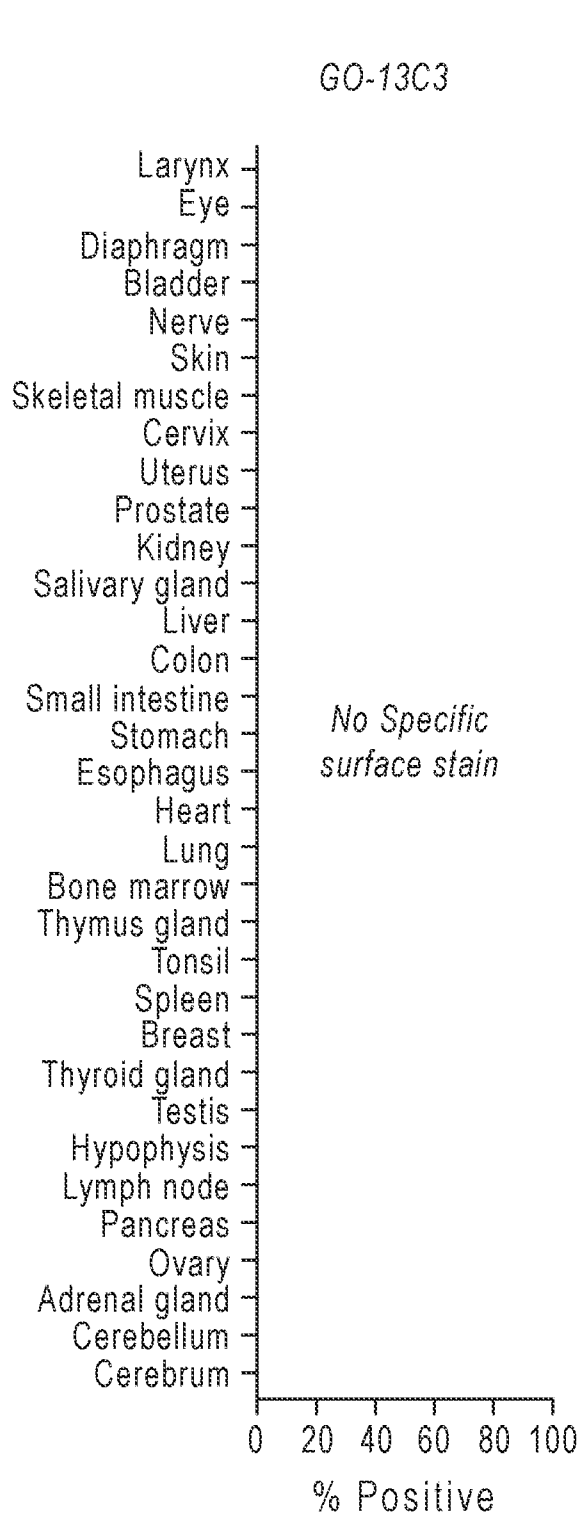


FIG. 4A-2

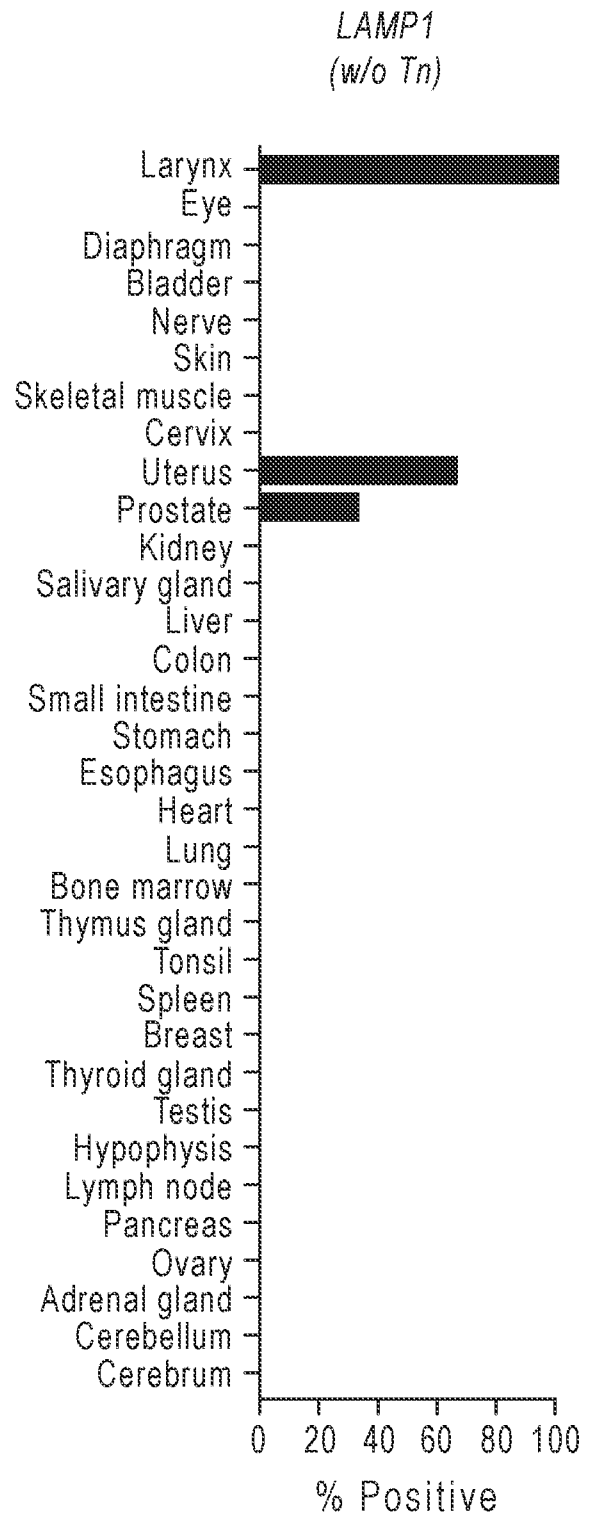


FIG. 4A-3

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Human Cancer Tissue

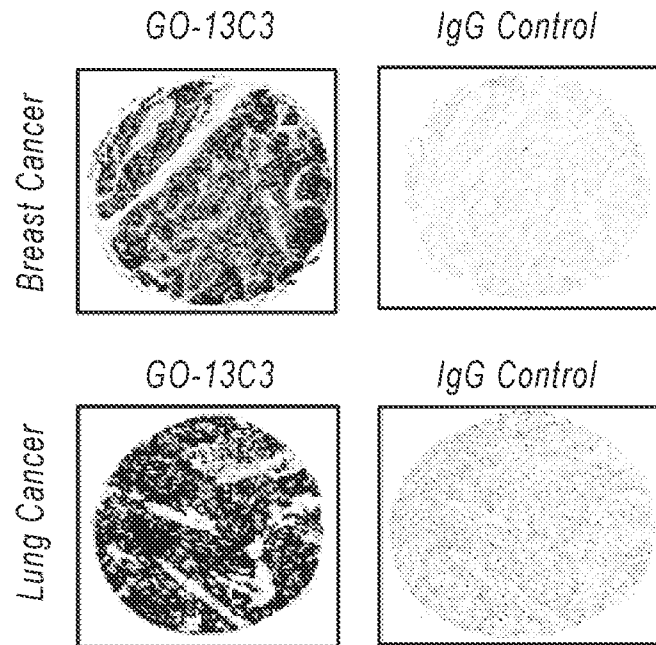


FIG. 4B-1

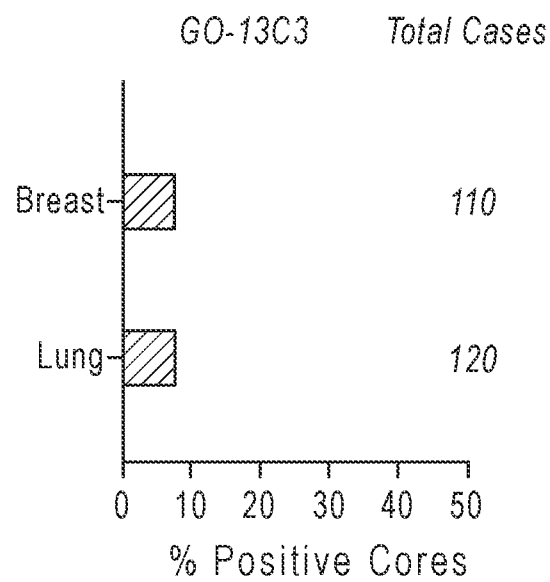


FIG. 4B-2

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LAMP1-DX8951 on T47D-COSMC-KO

FIG. 5A-1

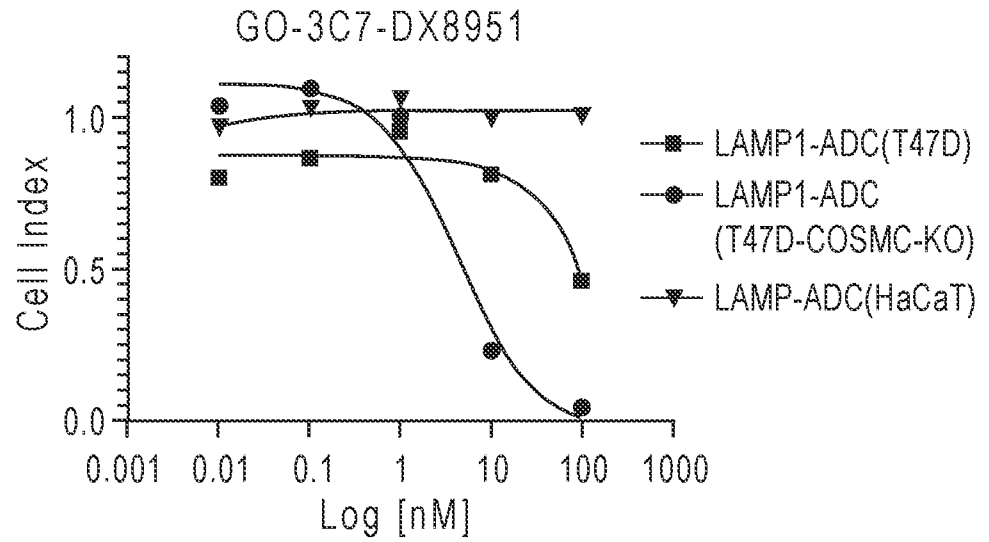


FIG. 5A-2

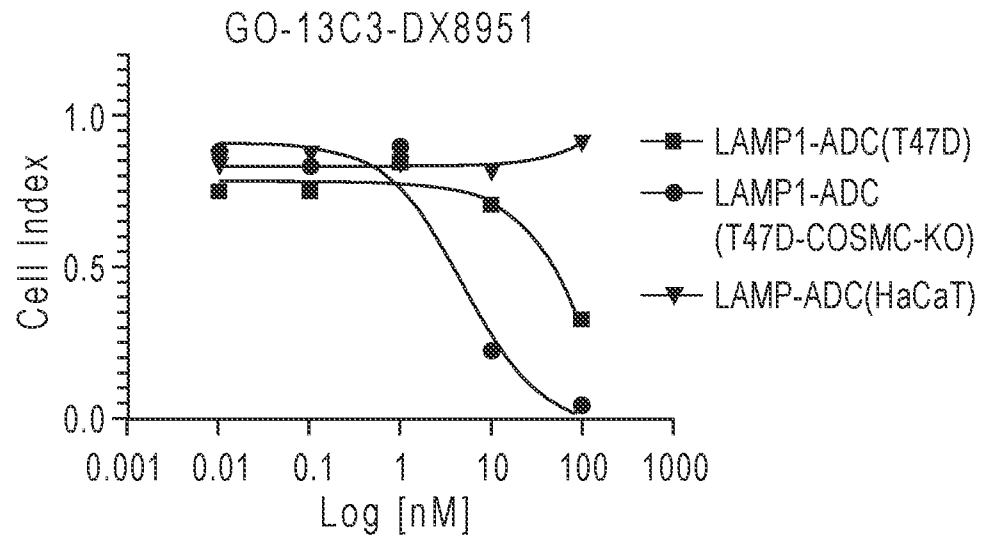
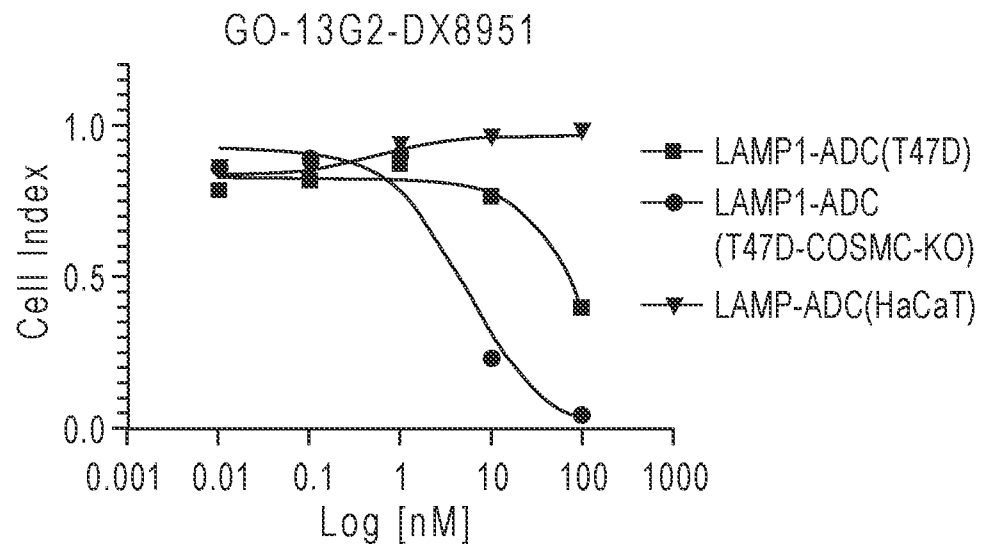


FIG. 5A-3



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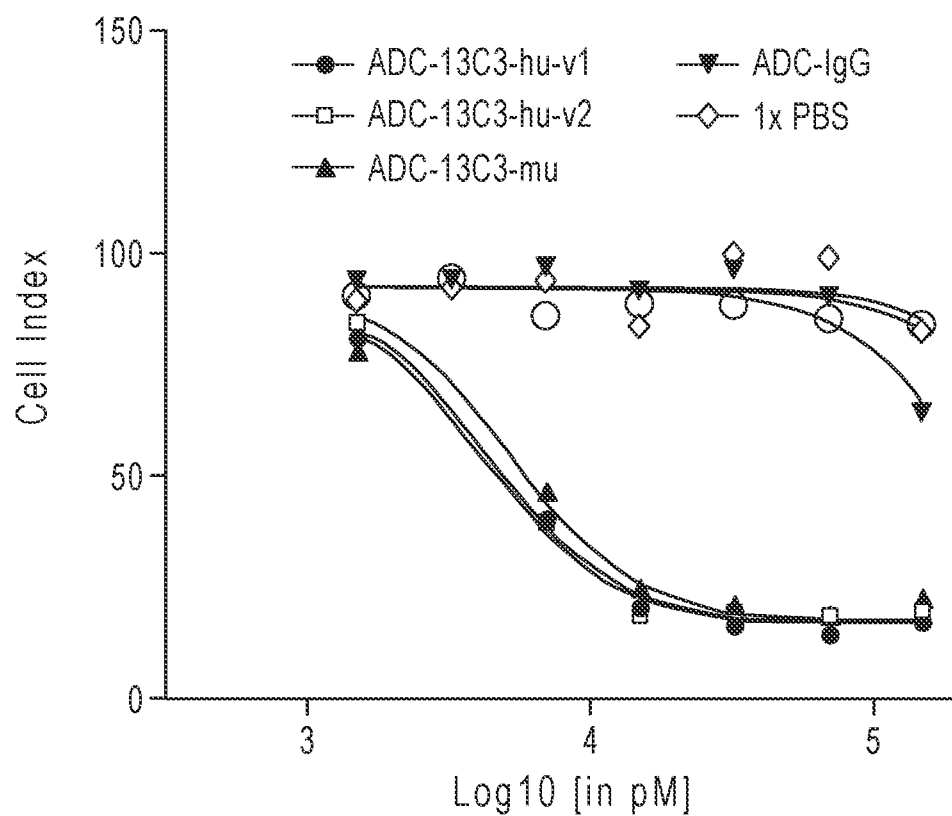
13C3-vc-PAB-MMAE on T47D-COSMC-KO

FIG. 5B

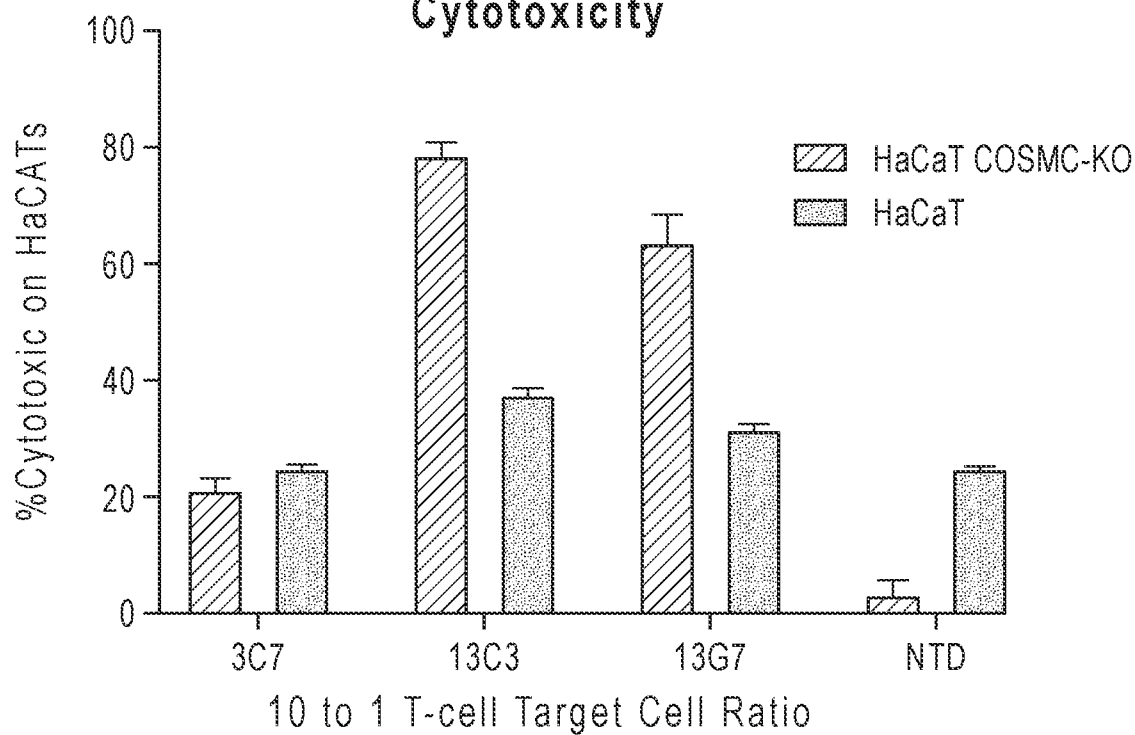
Cytotoxicity

FIG. 6

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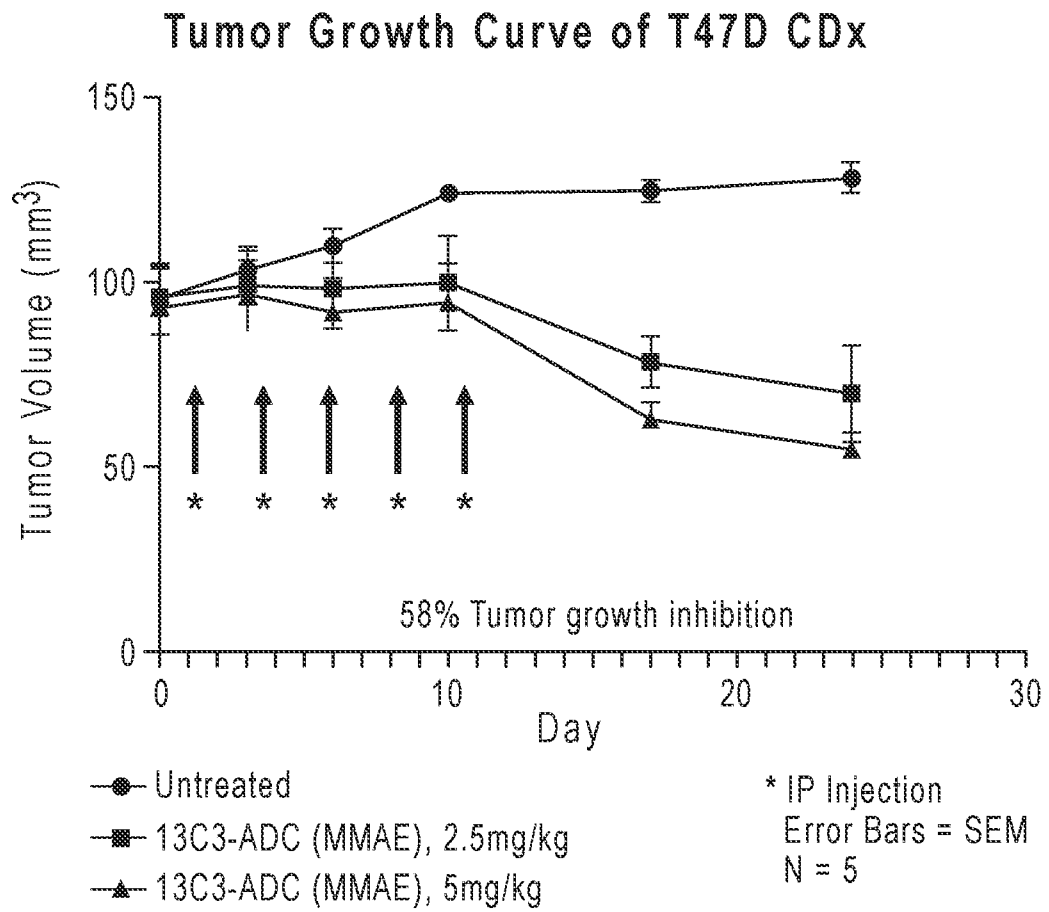


FIG. 7

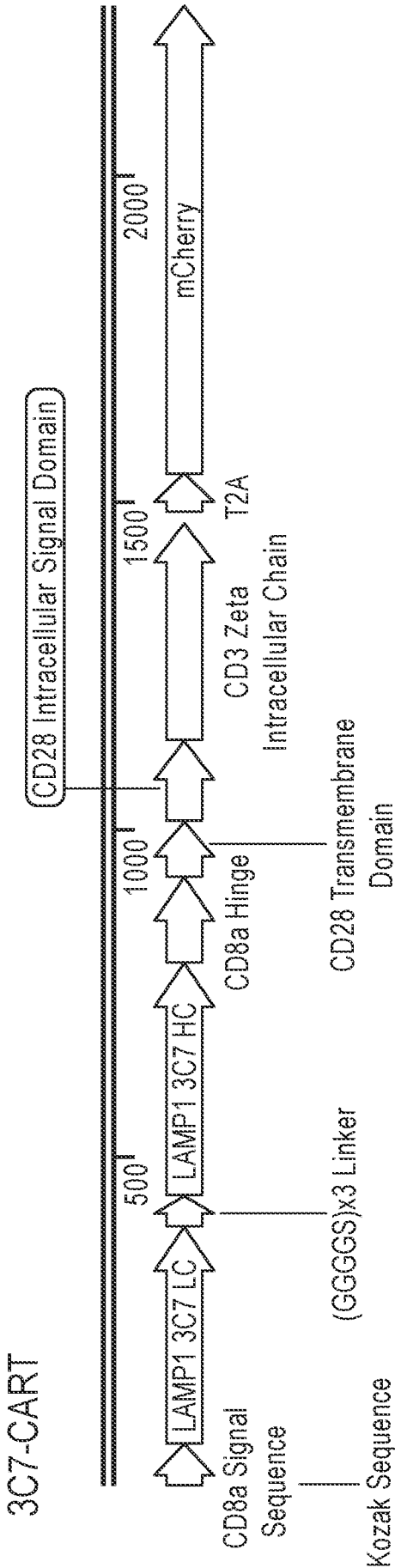


FIG. 8A

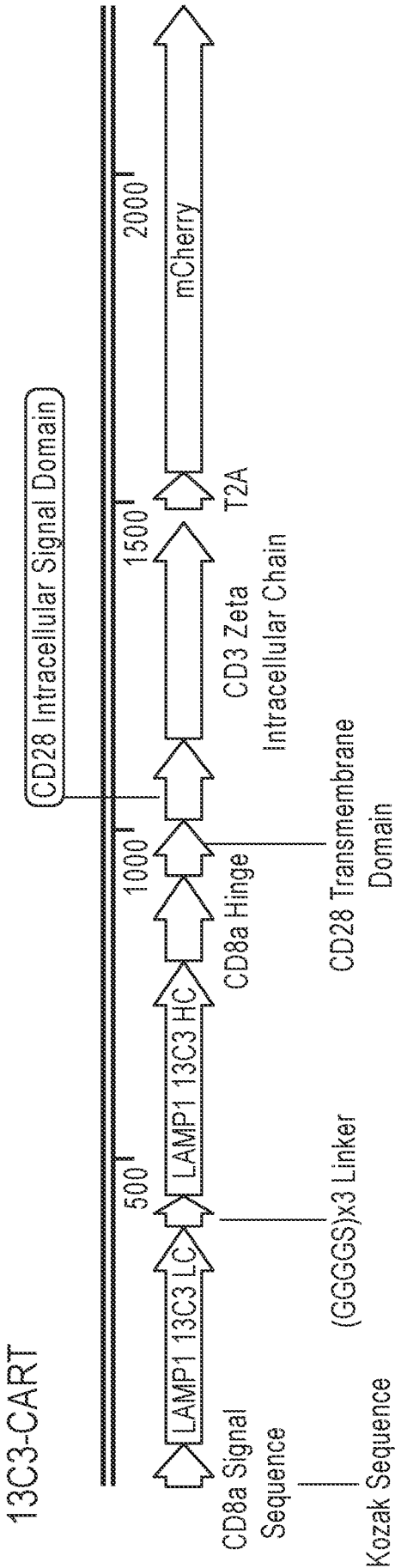


FIG. 8B

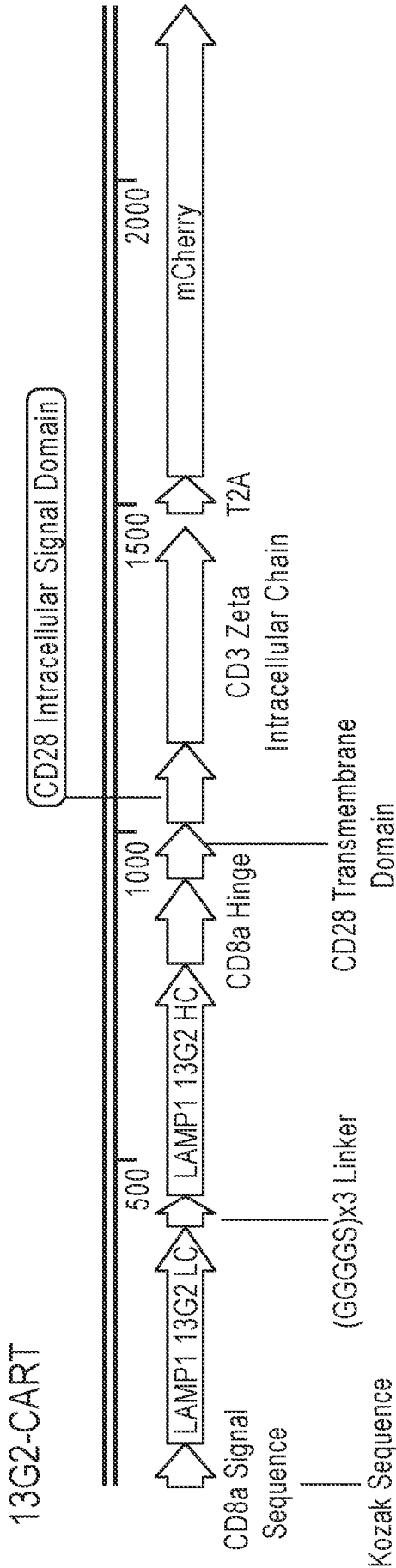


FIG. 8C

Heavy Chain

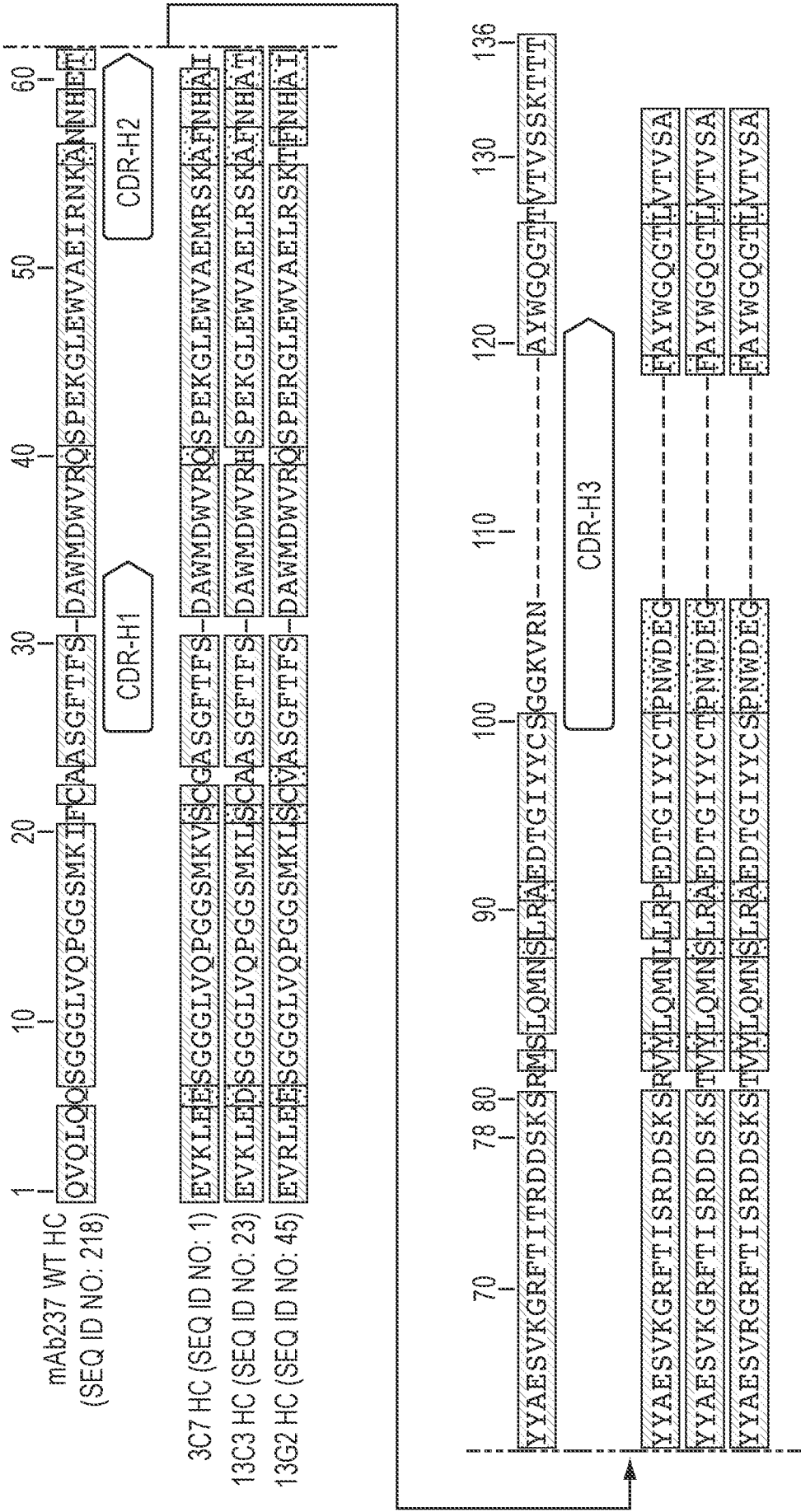


FIG. 9A

Light Chain

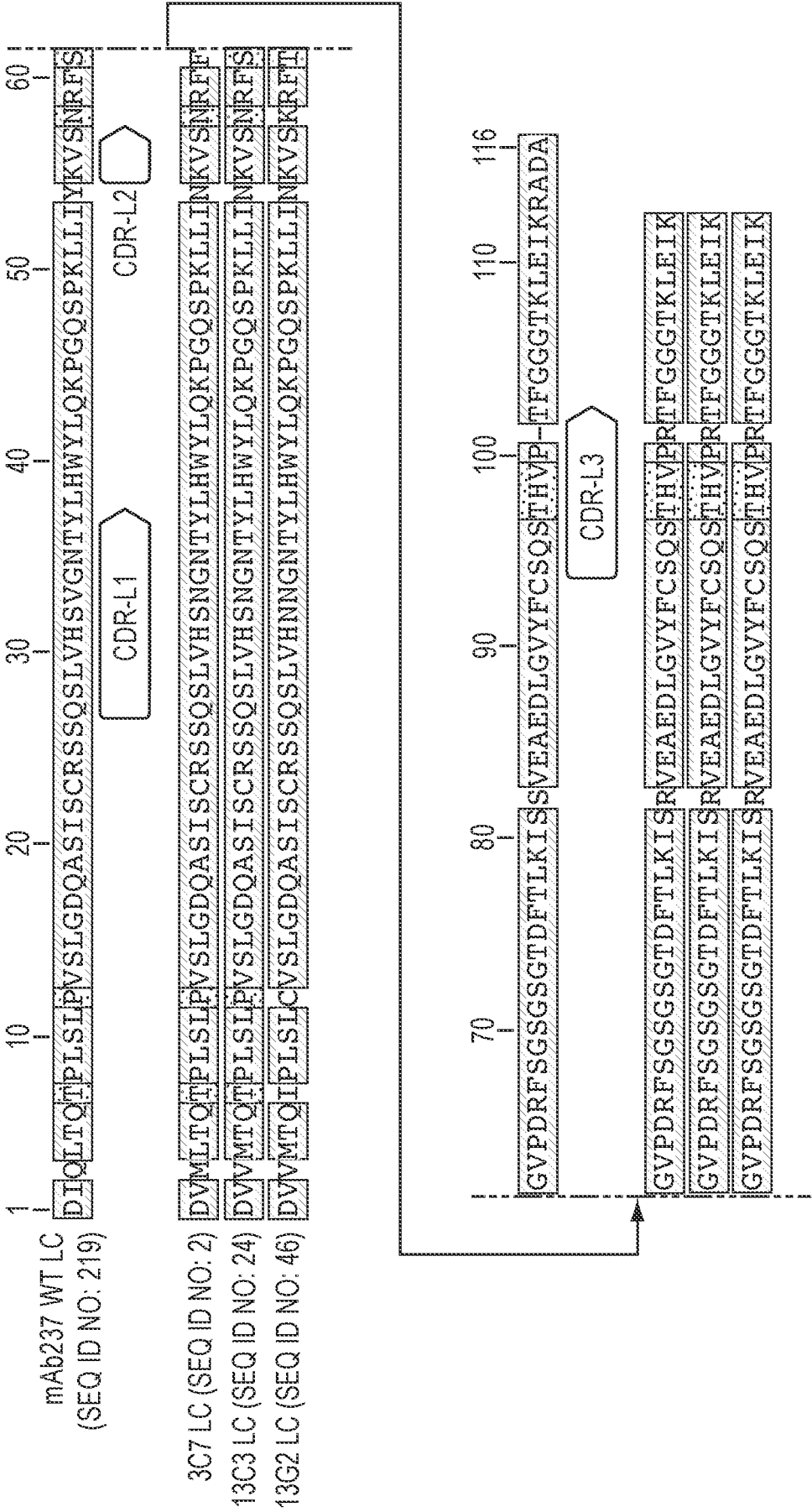


FIG. 9B

Overlay of Mouse mAbs on T47D COSMC-KO Cells

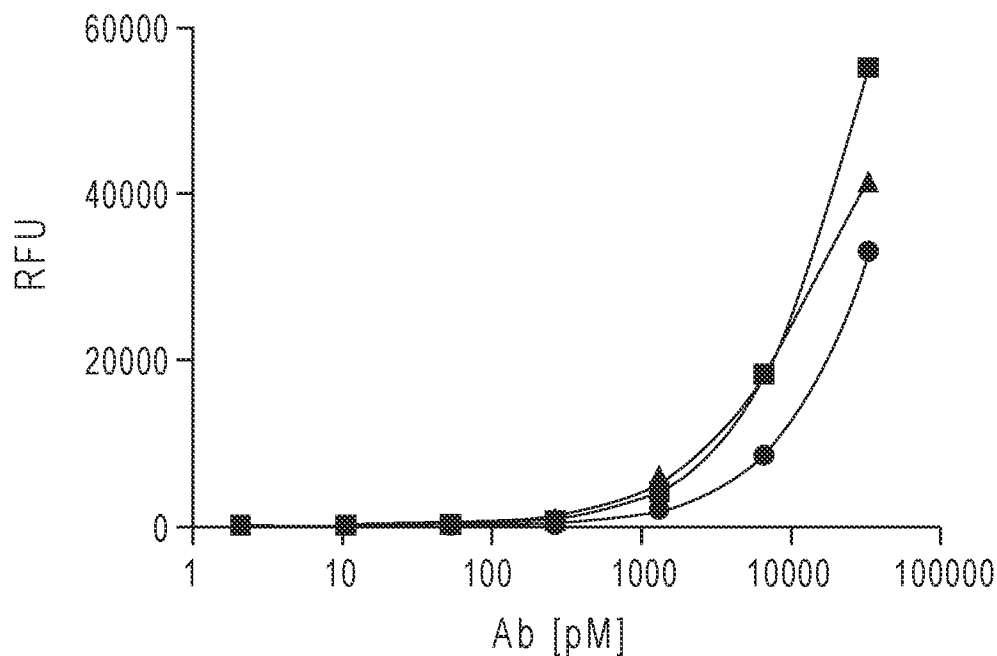


FIG. 1B-1