

Lp represents any one selected from the group consisting of:

-GGVA-, -GG-(D-)VA-, -VA-, -GGFG-, -GGPI-, -GGVCit-, -GGVK- and -GGPL-,

La represents any one selected from the group consisting of:

-C(=O)-CH₂CH₂-C(=O)-,

-C(=O)-(CH₂CH₂)₂-C(=O)-,

-C(=O)-CH₂CH₂-C(=O)-NH-(CH₂CH₂)₂-C(=O)-,

-C(=O)-CH₂CH₂-C(=O)-NH-(CH₂CH₂O)₂-CH₂-C(=O)-,

-C(=O)-CH₂CH₂-NH-C(=O)-(CH₂CH₂O)₄-CH₂CH₂-C(=O)-,

-CH₂-OC(=O)- and

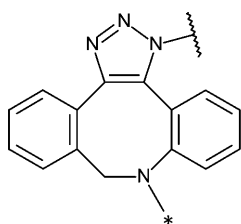
-OC(=O)-,

and

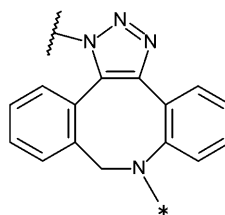
Lb represents the following formula:

[0024]

[Formula 4]

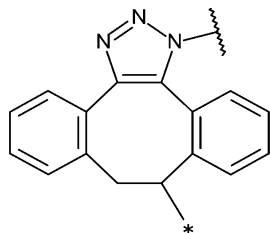


or

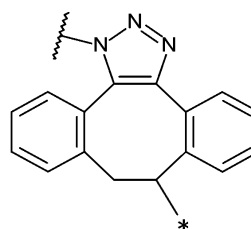


[0025]

[Formula 5]



or



amino acid sequence at positions 20 to 471 in SEQ ID NO: 69.

[52] An antibody or a functional fragment thereof having a light chain consisting of the amino acid sequence at positions 21 to 233 in SEQ ID NO: 31 and a heavy chain consisting of the amino acid sequence at positions 20 to 471 in SEQ ID NO: 65.

[53] A polynucleotide encoding the antibody according to any one of [46] to [52].

[0075]

[54] An expression vector containing the polynucleotide according to [53].

[55] A host cell transformed with the expression vector according to [54].

[56] A method for producing the antibody or a functional fragment thereof according to any one of [46] to [52], comprising a step of culturing the host cell according to [55] and collecting the targeted antibody from the culture obtained from the step of culturing.

[57] An antibody or a functional fragment thereof, obtained by the method according to [56].

[58] A pharmaceutical composition containing the antibody-drug conjugate according to any one of [1] to [42] and [45] or the antibody or a functional fragment thereof according to any one of [46] to [52] and [57].

[59] The pharmaceutical composition according to [58], which is an antitumor drug.

body of the animal thus immunized, so that an antibody against the antigen protein is produced therein.

[0111]

(2) Production of anti-CDH6 monoclonal antibody

The anti-CDH6 antibody used in the present invention is not particularly limited. For example, an antibody specified by an amino acid sequence shown in the sequence listing of the present application can suitably be used. The anti-CDH6 antibody used in the present invention is desirably an antibody having the following properties:

(1) an antibody having the following properties:

(a) specifically binding to CDH6, and

(b) having the activity of being internalized into CDH6-expressing cells by binding to CDH6;

(2) the antibody according to the above (1), wherein the CDH6 is human CDH6; or

(3) specifically recognizing EC3 of human CDH6, and having internalization activity.

[0112]

The method for obtaining the antibody against CDH6 of the present invention is not particularly limited as long as an anti-CDH6 antibody can be obtained. It is preferred to use CDH6 retaining its conformation as an antigen.

[0113]

antibody" or "chG019". The light chain full-length amino acid sequence of the chG019 antibody is encoded by the nucleotide sequence shown in SEQ ID NO: 24, and the heavy chain full-length amino acid sequence of the chG019 antibody is encoded by the nucleotide sequence shown in SEQ ID NO: 27.

[0129]

The amino acid sequence of the light chain variable region of the chG019 antibody is identical to the amino acid sequence of the light chain variable region of the rG019 antibody, and consists of the amino acid sequence shown in SEQ ID NO: 10. The light chain of the chG019 antibody has CDRL1 consisting of the amino acid sequence shown in SEQ ID NO: 12, CDRL2 consisting of the amino acid sequence shown in SEQ ID NO: 13, and CDRL3 consisting of the amino acid sequence shown in SEQ ID NO: 14, which are identical to the light chain CDRL1, CDRL2 and CDRL3, respectively, of rG019. The amino acid sequence of the light chain variable region of the chG019 antibody is encoded by the nucleotide sequence shown in SEQ ID NO: 25.

[0130]

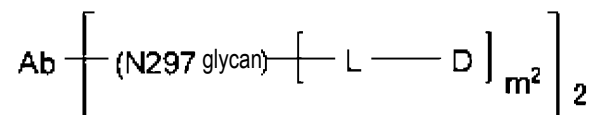
The amino acid sequence of the heavy chain variable region of the chG019 antibody consists of the amino acid sequence shown in SEQ ID NO: 28. The heavy chain of the chG019 antibody has CDRH1 consisting of the amino acid sequence shown in SEQ ID NO: 17, CDRH2 consisting of the

3. Anti-CDH6 antibody-drug conjugate

The antibody-drug conjugate of the present invention is represented by the following formula:

[0198]

[Formula 34]



[0199]

wherein

m^2 represents an integer of 1 or 2,

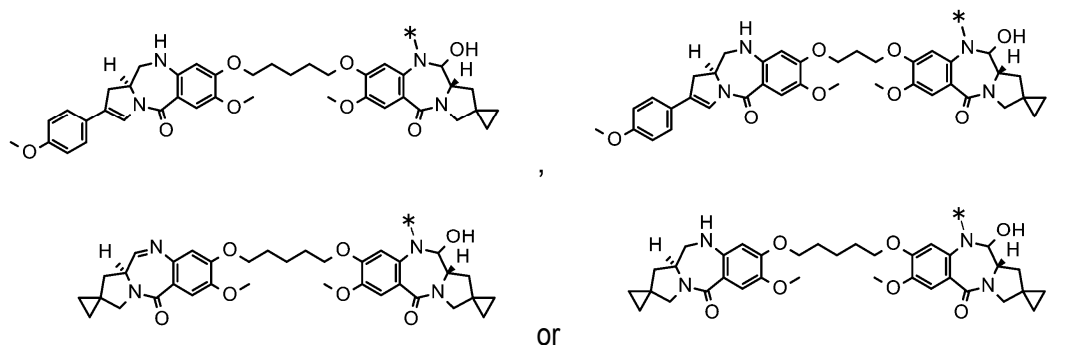
Ab represents an IgG antibody specifically binding to an amino acid sequence comprising the amino acid sequence shown in SEQ ID NO: 4 and having internalization ability that permits cellular uptake, or a functional fragment thereof

L represents a linker, linking the glycan bonding to N297 of Ab and D, and

D is any one of the following formulas:

[0200]

[Formula 35]



[0312]

[Expression 4]

ϵ_{280} = Molar absorption coefficient of antibody $\epsilon_{Ab, 280}$ +
Molar absorption coefficient of drug $\epsilon_{DL, 280}$ $\times$ Number of
drug molecules conjugated Expression (IV)

[0313]

Here, $\epsilon_{Ab, 280}$ denotes the molar absorption coefficient of an antibody at 280 nm and $\epsilon_{DL, 280}$ denotes the molar absorption coefficient of a drug at 280 nm.

By using a known calculation method (Protein Science, 1995, vol. 4, 2411-2423), $\epsilon_{Ab, 280}$ can be estimated from the amino acid sequence of an antibody. In the Examples, the molar absorption coefficient of H01L02 antibody used was $\epsilon_{Ab, 280} = 223400$ (calculated estimated value). The molar absorption coefficient of H01L02A antibody used was $\epsilon_{Ab, 280} = 223674$ (calculated estimated value), the molar absorption coefficient of H31L02A antibody used was $\epsilon_{Ab, 280} = 223314$ (calculated estimated value), the molar absorption coefficient of H11L02A antibody used was $\epsilon_{Ab, 280} = 220490$ (calculated estimated value), and the molar absorption coefficient of LPS antibody used was $\epsilon_{Ab, 280} = 230300$ (calculated estimated value).

$\epsilon_{DL, 280}$ was calculated for use from a measured value obtained in each UV measurement. Specifically, the absorbance of a solution dissolving a conjugate precursor (drug linker) with a certain molarity was measured, and

in a medium supplemented with G418 (Gibco) (final concentration: 50 mg/mL) and screened with the drug, so as to establish cell line 786-O/hCDH6 stably expressing human CDH6. The high expression of human CDH6 in the stably expressing line was confirmed by flow cytometry in the same manner as that applied in Example 2)-3-1 (Figure 6). Goat anti-Mouse IgG1 Secondary Antibody Alexa Fluor 647 (Thermo Fisher Scientific Inc.) that had been 500-fold diluted with PBS supplemented with 5% FBS was used as an antibody for detection. The results are shown in Figure 6. In the histogram of Figure 6, the abscissa depicts Alexa Fluor 647 fluorescence intensity indicating the amount of the antibody bound, and the ordinate depicts cell count. The shaded histogram shows that the negative control mIgG1 was used in staining, and the open solid line histogram shows that the anti-human CDH6 antibody was used in staining. As seen, fluorescence intensity was enhanced by the binding of the antibody to hCDH6 on cell surface. The mIgG1 control binds to none of the cells. As a result, it was demonstrated that the 786-O/hCDH6 stably expressing cell line more highly expresses human CDH6 than the parent line 786-O cells.

[0396]

6)-2-2-2 Binding Competition assay using labeled H01L02 and labeled NOV0712

Labeled H01L02 and labeled NOV0712 were produced using an Alexa Fluor 488 Monoclonal Antibody Labeling Kit

Step 7: (11aS)-8-(3-Bromopropoxy)-7-methoxy-2-(4-methoxyphenyl)-1,10,11,11a-tetrahydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-5-one (4-7)

The compound obtained in step 6 (4-6) (1.59 g, 3.38 mmol) was reacted in the same manner as in step 8 of Example 10-3 to afford the desired compound (4-7) (1.39 g, 87%).

¹H-NMR (CDCl₃) δ: 7.54 (1H, s), 7.54-7.51 (1H, m), 7.32-7.29 (2H, m), 6.89-6.87 (2H, m), 6.10 (1H, s), 4.32-4.28 (2H, m), 4.14-4.13 (2H, m), 3.85 (3H, s), 3.82 (3H, s), 3.63-3.62 (2H, m), 3.57-3.55 (2H, m), 3.40-3.36 (1H, m), 2.76-2.72 (1H, m), 2.40-2.37 (2H, m).

MS (APCI, ESI) m/z: 475 [81Br, (M+H)+], 473 [79Br, (M+H)+].

[0448]

Step 8: Prop-2-en-1-yl (11aS)-8-(3-bromopropoxy)-7-methoxy-2-(4-methoxyphenyl)-5-oxo-11,11a-dihydro-1H-pyrrolo[2,1-c][1,4]benzodiazepin-10(5H)-carboxylate (4-8)

The compound obtained in step 7 (4-7) (1.40 g, 0.295 mmol) was reacted in the same manner as in step 9 of Example 10-3 to afford the desired compound (4-8) (0.885 g, 54%).

¹H-NMR (CDCl₃) δ: 7.34 (1H, s), 7.27-7.25 (2H, m), 7.22 (1H, s), 6.86-6.84 (2H, m), 6.73 (1H, s), 5.76-5.74 (1H, m), 5.11-5.09 (2H, m), 4.62-4.59 (2H, m), 4.33-4.31 (1H, m), 4.16-4.13 (3H, m), 3.88 (3H, s), 3.79 (3H, s), 3.60-

(3H, m), 2.39 (1H, m), 1.95-1.90 (4H, m), 1.68-1.61 (3H, m), 1.44 (1H, m), 0.75-0.66 (4H, m).

[0476]

Step 9: N-[(Prop-2-en-1-yloxy)carbonyl]-L-valyl-N-{4-[[({[(11a'S)-11'-{[tert-butyl(dimethyl)silyl]oxy}-7'-methoxy-8'-{[5-({(11a'S)-7'-methoxy-5'-oxo-10'-[(prop-2-en-1-yloxy)carbonyl]-5',10',11',11a'-tetrahydro-1'H,3'H-spiro[cyclopropane-1,2'-pyrrolo[2,1-c][1,4]benzodiazepine]-8'-yl}oxy)pentyl]oxy}-5'-oxo-11',11a'-dihydro-1'H-spiro[cyclopropane-1,2'-pyrrolo[2,1-c][1,4]benzodiazepine]-10'(5'H)-yl]carbonyl}oxy)methyl]phenyl}-L-alaninamide (6-10)

The compound obtained in step 8 (6-9) (0.374 g, 0.737 mmol) was reacted with the compound obtained in step 10 of Example 10-1 (1-11) (0.452 g, 0.56 mmol) in the same manner as in step 10 of Example 10-3 to afford the desired compound (6-10) (0.589 g, 65%).

MS (APCI, ESI) m/z: 1234 (M+H)+

[0477]

Step 10: N-[(Prop-2-en-1-yloxy)carbonyl]-L-valyl-N-{4-[[({[(11a'S)-11'-hydroxy-7'-methoxy-8'-{[5-({(11a'S)-7'-methoxy-5'-oxo-10'-[(prop-2-en-1-yloxy)carbonyl]-5',10',11',11a'-tetrahydro-1'H-spiro[cyclopropane-1,2'-pyrrolo[2,1-c][1,4]benzodiazepine]-8'-yl}oxy)pentyl]oxy}-5'-oxo-11',11a'-dihydro-1'H-spiro[cyclopropane-1,2'-pyrrolo[2,1-c][1,4]benzodiazepine]-10'(5'H)-yl]carbonyl}oxy)methyl]phenyl}-L-alaninamide (6-11)

results are shown in Figure 12. The abscissa depicts the number of days after administration, and the ordinate depicts tumor volume. The error range depicts a SE value.

[0629]

In this tumor model, ADC6 exhibited the strongest anti-tumor effect, ADC1 and ADC5 exhibited almost the same second strongest anti-tumor effect. From this, it was shown that substitution of leucine residues at positions 234 and 235 (specified based on the EU index) of a human-antibody heavy chain with alanine residues hardly at all affects the anti-tumor effect of an antibody-drug conjugate. ADC11 as a control did not exhibit an anti-tumor effect at a dose of 0.4 mg/kg (Figure 12). From this, it was shown that the antitumor effects exhibited by ADC1, ADC5 and ADC6 are specifically obtained depending on the expression of CDH6 in tumor cells. It was confirmed that there is no weight loss in all drug administration groups, compared to the control group (the ABS buffer administration group).

[0630]

30)-4 Anti-tumor effect (4)

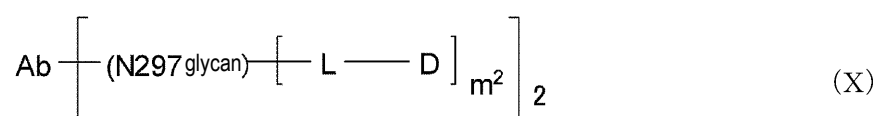
The CDH6-positive human ovarian tumor cell line OV-90 (ATCC), the CDH6 expression of which had been confirmed in Example 2)-3, was suspended in Matrigel (Corning Inc.), and the cell suspension was subcutaneously inoculated at a dose of 2.5×10^6 cells to

Claims

[Claim 1]

An antibody-drug conjugate represented by the following formula (X):

[Formula 1]



wherein m^2 represents an integer of 1 or 2,

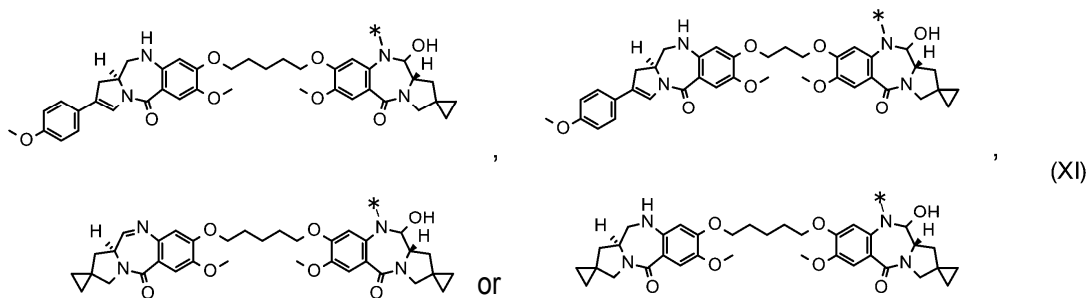
Ab represents an IgG antibody specifically binding to an amino acid sequence comprising the amino acid sequence shown in SEQ ID NO: 4 and having internalization ability that permits cellular uptake, or a functional fragment thereof,

L represents a linker linking a glycan bonding to N297 of Ab (N297 glycan) and D,

N297 glycan may be a remodeled glycan, and

D is any one of the following formulas:

[Formula 2]



wherein the asterisk (*) represents bonding to L.

[Claim 2]

The antibody-drug conjugate according to claim 1, wherein the antibody or a functional fragment thereof exhibits competitive inhibitory activity, for binding to the amino acid sequence comprising the amino acid sequence shown in SEQ ID NO: 4, against at least any one antibody selected from the group consisting of the following antibodies (1) to (8):

(1) an antibody having a light chain consisting of the amino acid sequence at positions 21 to 233 in SEQ ID NO: 23 and a heavy chain consisting of the amino acid sequence at positions 20 to 471 in SEQ ID NO: 26,

(2) an antibody having a light chain consisting of the amino acid sequence at positions 21 to 233 in SEQ ID NO: 31 and a heavy chain consisting of the amino acid sequence at positions 20 to 471 in SEQ ID NO: 39,

(3) an antibody having a light chain consisting of the amino acid sequence at positions 21 to 233 in SEQ ID NO: 31 and a heavy chain consisting of the amino acid sequence at positions 20 to 471 in SEQ ID NO: 43,

(4) an antibody having a light chain consisting of the amino acid sequence at positions 21 to 233 in SEQ ID NO: 35 and a heavy chain consisting of the amino acid sequence at positions 20 to 471 in SEQ ID NO: 43,

(5) an antibody having a light chain consisting of the amino acid sequence at positions 21 to 233 in SEQ ID

NO: 31 and a heavy chain consisting of the amino acid sequence at positions 20 to 471 in SEQ ID NO: 47,

(6) an antibody having a light chain consisting of the amino acid sequence at positions 21 to 233 in SEQ ID NO: 31 and a heavy chain consisting of the amino acid sequence at positions 20 to 471 in SEQ ID NO: 65,

(7) an antibody having a light chain consisting of the amino acid sequence at positions 21 to 233 in SEQ ID NO: 31 and a heavy chain consisting of the amino acid sequence at positions 20 to 471 in SEQ ID NO: 67, and

(8) an antibody having a light chain consisting of the amino acid sequence at positions 21 to 233 in SEQ ID NO: 31 and a heavy chain consisting of the amino acid sequence at positions 20 to 471 in SEQ ID NO: 69.

[Claim 3]

The antibody-drug conjugate according to claim 1 or 2, wherein the antibody or a functional fragment thereof comprises CDRL1, CDRL2 and CDRL3; and CDRH1, CDRH2 and CDRH3 selected from the group consisting of the following (1) to (4):

(1) CDRL1 consisting of the amino acid sequence shown in SEQ ID NO: 12, CDRL2 consisting of the amino acid sequence shown in SEQ ID NO: 13 and CDRL3 consisting of the amino acid sequence shown in SEQ ID NO: 14; and CDRH1 consisting of the amino acid sequence shown in SEQ ID NO: 17, CDRH2 consisting of the amino acid sequence

shown in SEQ ID NO: 18 and CDRH3 consisting of the amino acid sequence shown in SEQ ID NO: 19,

(2) CDRL1 consisting of the amino acid sequence shown in SEQ ID NO: 12, CDRL2 consisting of the amino acid sequence shown in SEQ ID NO: 13 and CDRL3 consisting of the amino acid sequence shown in SEQ ID NO: 14; and CDRH1 consisting of the amino acid sequence shown in SEQ ID NO: 17, CDRH2 consisting of the amino acid sequence shown in SEQ ID NO: 30 and CDRH3 consisting of the amino acid sequence shown in SEQ ID NO: 19,

(3) CDRL1 consisting of the amino acid sequence shown in SEQ ID NO: 12, CDRL2 consisting of the amino acid sequence shown in SEQ ID NO: 13 and CDRL3 consisting of the amino acid sequence shown in SEQ ID NO: 14; and CDRH1 consisting of the amino acid sequence shown in SEQ ID NO: 57, CDRH2 consisting of the amino acid sequence shown in SEQ ID NO: 58 and CDRH3 consisting of the amino acid sequence shown in SEQ ID NO: 59, and

(4) CDRL1 consisting of the amino acid sequence shown in SEQ ID NO: 12, CDRL2 consisting of the amino acid sequence shown in SEQ ID NO: 13 and CDRL3 consisting of the amino acid sequence shown in SEQ ID NO: 14 and CDRH1 consisting of the amino acid sequence shown in SEQ ID NO: 62, CDRH2 consisting of the amino acid sequence shown in SEQ ID NO: 63 and CDRH3 consisting of the amino acid sequence shown in SEQ ID NO: 64.

[Claim 4]

The antibody-drug conjugate according to any one of claims 1 to 3, wherein the antibody or a functional fragment thereof comprises any one light chain variable region selected from the group consisting of the following variable regions (1) to (4):

(1) a light chain variable region consisting of the amino acid sequence shown in SEQ ID NO: 33,

(2) a light chain variable region consisting of the amino acid sequence shown in SEQ ID NO: 37,

(3) an amino acid sequence having a sequence identity of at least 95% to the sequence of a framework region except CDR sequences in the amino acid sequence of (1) or (2) and

(4) an amino acid sequence having a deletion, substitution or addition of one or several amino acids in the sequence of a framework region except CDR sequences in the amino acid sequences of (1) to (3); and

any one heavy chain variable region selected from the group consisting of the following variable regions (5) to (11):

(5) a heavy chain variable region consisting of the amino acid sequence shown in SEQ ID NO: 41,

(6) a heavy chain variable region consisting of the amino acid sequence shown in SEQ ID NO: 45,

(7) a heavy chain variable region consisting of the amino acid sequence shown in SEQ ID NO: 49,

(8) a heavy chain variable region consisting of the amino acid sequence shown in SEQ ID NO: 55,

(9) a heavy chain variable region consisting of the amino acid sequence shown in SEQ ID NO: 60,

(10) an amino acid sequence having a sequence identity of at least 95% to the sequence of a framework region other than at each CDR sequence in the amino acid sequences of (5) to (9), and

(11) an amino acid sequence having a deletion, substitution or addition of one or several amino acids in the sequence of a framework region other than at each CDR sequence in the amino acid sequences of (5) to (10).

[Claim 5]

The antibody-drug conjugate according to any one of claims 1 to 4, wherein the antibody or a functional fragment thereof comprises any one of the following (1) to (6):

(1) a light chain variable region consisting of the amino acid sequence shown in SEQ ID NO: 33 and a heavy chain variable region consisting of the amino acid sequence shown in SEQ ID NO: 41,

(2) a light chain variable region consisting of the amino acid sequence shown in SEQ ID NO: 33 and a heavy chain variable region consisting of the amino acid sequence shown in SEQ ID NO: 45,

(3) a light chain variable region consisting of the amino acid sequence shown in SEQ ID NO: 37 and a heavy

chain variable region consisting of the amino acid sequence shown in SEQ ID NO: 45,

(4) a light chain variable region consisting of the amino acid sequence shown in SEQ ID NO: 33 and a heavy chain variable region consisting of the amino acid sequence shown in SEQ ID NO: 49,

(5) a light chain variable region consisting of the amino acid sequence shown in SEQ ID NO: 33 and a heavy chain variable region consisting of the amino acid sequence shown in SEQ ID NO: 55, and

(6) a light chain variable region consisting of the amino acid sequence shown in SEQ ID NO: 33 and a heavy chain variable region consisting of the amino acid sequence shown in SEQ ID NO: 60.

[Claim 6]

The antibody-drug conjugate according to any one of claims 1 to 5, wherein the antibody or a functional fragment thereof has any one of the following (1) to (7):

(1) a light chain consisting of the amino acid sequence at positions 21 to 233 in SEQ ID NO: 31 and a heavy chain consisting of the amino acid sequence at positions 20 to 471 in SEQ ID NO: 39,

(2) a light chain consisting of the amino acid sequence at positions 21 to 233 in SEQ ID NO: 31 and a heavy chain consisting of the amino acid sequence at positions 20 to 471 in SEQ ID NO: 43,

(3) a light chain consisting of the amino acid sequence at positions 21 to 233 in SEQ ID NO: 35 and a heavy chain consisting of the amino acid sequence at positions 20 to 471 in SEQ ID NO: 43,

(4) a light chain consisting of the amino acid sequence at positions 21 to 233 in SEQ ID NO: 31 and a heavy chain consisting of the amino acid sequence at positions 20 to 471 in SEQ ID NO: 47,

(5) a light chain consisting of the amino acid sequence at positions 21 to 233 in SEQ ID NO: 31 and a heavy chain consisting of the amino acid sequence at positions 20 to 471 in SEQ ID NO: 65,

(6) a light chain consisting of the amino acid sequence at positions 21 to 233 in SEQ ID NO: 31 and a heavy chain consisting of the amino acid sequence at positions 20 to 471 in SEQ ID NO: 67, and

(7) a light chain consisting of the amino acid sequence at positions 21 to 233 in SEQ ID NO: 31 and a heavy chain consisting of the amino acid sequence at positions 20 to 471 in SEQ ID NO: 69.

[Claim 7]

The antibody-drug conjugate according to claim 6, wherein the antibody or a functional fragment thereof has a light chain consisting of the amino acid sequence at positions 21 to 233 in SEQ ID NO: 31 and a heavy chain consisting of the amino acid sequence at positions 20 to 471 in SEQ ID NO: 39.

[Claim 8]

The antibody-drug conjugate according to claim 6, wherein the antibody or a functional fragment thereof has a light chain consisting of the amino acid sequence at positions 21 to 233 in SEQ ID NO: 31 and a heavy chain consisting of the amino acid sequence at positions 20 to 471 in SEQ ID NO: 43.

[Claim 9]

The antibody-drug conjugate according to claim 6, wherein the antibody or a functional fragment thereof has a light chain consisting of the amino acid sequence at positions 21 to 233 in SEQ ID NO: 35 and a heavy chain consisting of the amino acid sequence at positions 20 to 471 in SEQ ID NO: 43.

[Claim 10]

The antibody-drug conjugate according to claim 6, wherein the antibody or a functional fragment thereof has a light chain consisting of the amino acid sequence at positions 21 to 233 in SEQ ID NO: 31 and a heavy chain consisting of the amino acid sequence at positions 20 to 471 in SEQ ID NO: 47.

[Claim 11]

The antibody-drug conjugate according to claim 6, wherein the antibody or a functional fragment thereof has a light chain consisting of the amino acid sequence at positions 21 to 233 in SEQ ID NO: 31 and a heavy chain

consisting of the amino acid sequence at positions 20 to 471 in SEQ ID NO: 65.

[Claim 12]

The antibody-drug conjugate according to claim 6, wherein the antibody or a functional fragment thereof has a light chain consisting of the amino acid sequence at positions 21 to 233 in SEQ ID NO: 31 and a heavy chain consisting of the amino acid sequence at positions 20 to 471 in SEQ ID NO: 67.

[Claim 13]

The antibody-drug conjugate according to claim 6, wherein the antibody or a functional fragment thereof has a light chain consisting of the amino acid sequence at positions 21 to 233 in SEQ ID NO: 31 and a heavy chain consisting of the amino acid sequence at positions 20 to 471 in SEQ ID NO: 69.

[Claim 14]

The antibody-drug conjugate according to any one of claims 1 to 13, wherein

L is represented by $-L_b-L_a-L_p-NH-B-CH_2-O(C=O)-*$, wherein the asterisk * represents bonding to the nitrogen atom at the N10'-position of D,

B represents a 1,4-phenyl group, a 2,5-pyridyl group, a 3,6-pyridyl group, a 2,5-pyrimidyl group or a 2,5-thienyl group,

Lp represents any one selected from the group consisting of:

-GGVA-, -GG-(D-)VA-, -VA-, -GGFG-, -GGPI-, -GGVCit-, -GGVK- and -GGPL-,

La represents any one selected from the group consisting of:

-C(=O)-CH₂CH₂-C(=O)-,

-C(=O)-(CH₂CH₂)₂-C(=O)-,

-C(=O)-CH₂CH₂-C(=O)-NH-(CH₂CH₂)₂-C(=O)-,

-C(=O)-CH₂CH₂-C(=O)-NH-(CH₂CH₂O)₂-CH₂-C(=O)-,

-C(=O)-CH₂CH₂-NH-C(=O)-(CH₂CH₂O)₄-CH₂CH₂-C(=O)-,

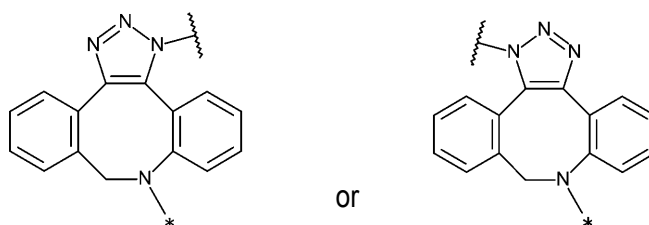
-CH₂-OC(=O)- and

-OC(=O)-,

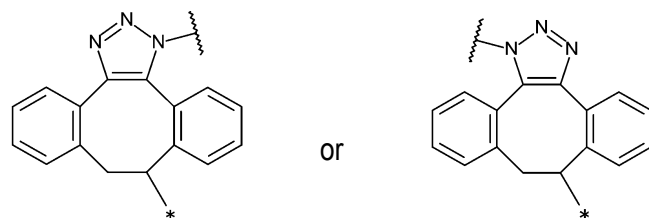
and

Lb represents the following formula:

[Formula 4]

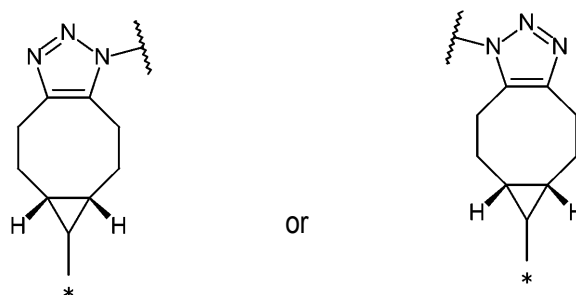


[Formula 5]



or

[Formula 6]



wherein, in each structural formula of Lb shown above, each asterisk * represents bonding to La, and each wavy line represents bonding to the glycan presented by Ab or a remodeled glycan.

[Claim 15]

The antibody-drug conjugate according to any one of claims 1 to 14, wherein

L represents any one selected from the group consisting of the following structural formulas:

-Z¹-C(=O)-CH₂CH₂-C(=O)-GGVA-NH-B-CH₂-OC(=O)-,
 -Z¹-C(=O)-CH₂CH₂-C(=O)-GG-(D-)VA-NH-B-CH₂-OC(=O)-,
 -Z¹-C(=O)-CH₂CH₂-C(=O)-VA-NH-B-CH₂-OC(=O)-,
 -Z¹-C(=O)-(CH₂CH₂)₂-C(=O)-VA-NH-B-CH₂-OC(=O)-,
 -Z¹-C(=O)-CH₂CH₂-C(=O)-GGPI-NH-B-CH₂-OC(=O)-,
 -Z¹-C(=O)-CH₂CH₂-C(=O)-GGFG-NH-B-CH₂-OC(=O)-,
 -Z¹-C(=O)-CH₂CH₂-C(=O)-GGVCit-NH-B-CH₂-OC(=O)-,
 -Z¹-C(=O)-CH₂CH₂-C(=O)-GGVK-NH-B-CH₂-OC(=O)-,
 -Z¹-C(=O)-CH₂CH₂-C(=O)-GGPL-NH-B-CH₂-OC(=O)-,
 -Z¹-C(=O)-CH₂CH₂-C(=O)-NH-(CH₂CH₂)₂-C(=O)-VA-NH-B-CH₂-
 OC(=O)-,

$-Z^1-C(=O)-CH_2CH_2-C(=O)-NH-(CH_2CH_2O)_2-CH_2-C(=O)-VA-NH-B-CH_2-OC(=O)-$,

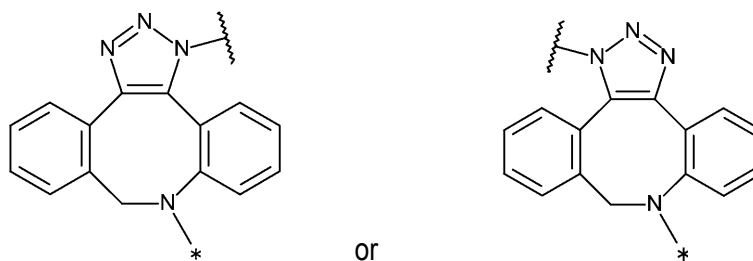
$-Z^1-C(=O)-CH_2CH_2-NH-C(=O)-(CH_2CH_2O)_4-CH_2CH_2-C(=O)-VA-NH-B-CH_2-OC(=O)-$,

$-Z^2-OC(=O)-GGVA-NH-B-CH_2-OC(=O)-$ and

$-Z^3-CH_2-OC(=O)-GGVA-NH-B-CH_2-OC(=O)-$

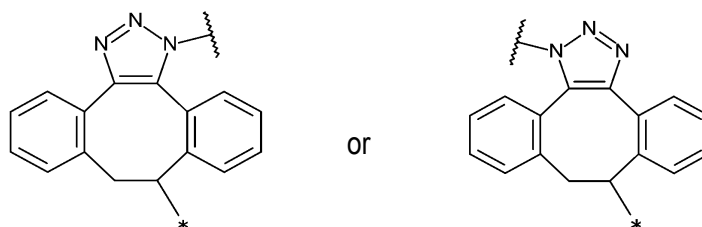
wherein Z^1 represents the following structural formula:

[Formula 7]



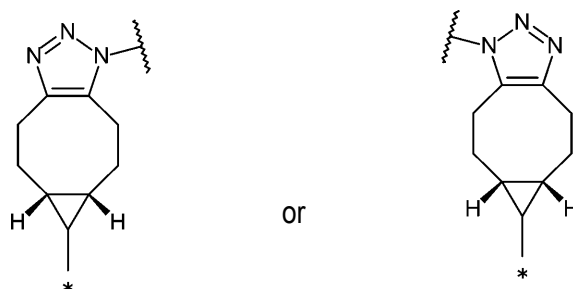
Z^2 represents the following structural formula:

[Formula 8]



Z^3 represents the following structural formula:

[Formula 9]



wherein, in each structural formula represented for Z^1 , Z^2 and Z^3 , each asterisk * represents bonding to the C(=O), O or CH₂ neighboring Z^1 , Z^2 or Z^3 ; each wavy line represents bonding to the glycan presented by Ab or a remodeled glycan, and

B represents a 1,4-phenyl group.

[Claim 16]

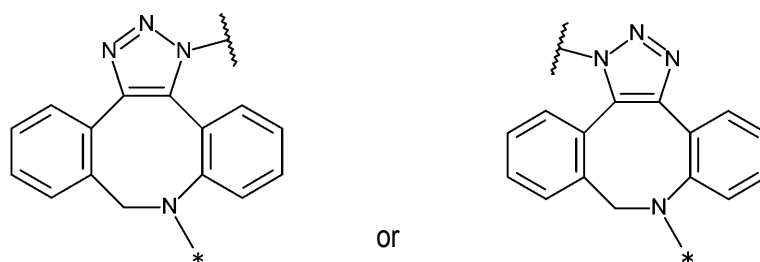
The antibody-drug conjugate according to any one of claims 1 to 15, wherein

L represents any one selected from the group consisting of:

- Z^1 -C(=O)-CH₂CH₂-C(=O)-GGVA-NH-B-CH₂-OC(=O)-,
- Z^1 -C(=O)-CH₂CH₂-C(=O)-VA-NH-B-CH₂-OC(=O)-,
- Z^1 -C(=O)-(CH₂CH₂)₂-C(=O)-VA-NH-B-CH₂-OC(=O)-,
- Z^1 -C(=O)-CH₂CH₂-C(=O)-GGVCit-NH-B-CH₂-OC(=O)-, - Z^1 -C(=O)-CH₂CH₂-C(=O)-NH-(CH₂CH₂)₂-C(=O)-VA-NH-B-CH₂-OC(=O)-,
- Z^1 -C(=O)-CH₂CH₂-C(=O)-NH-(CH₂CH₂O)₂-CH₂-C(=O)-VA-NH-B-CH₂-OC(=O)- and
- Z^1 -C(=O)-CH₂CH₂-NH-C(=O)-(CH₂CH₂O)₄-CH₂CH₂-C(=O)-VA-NH-B-CH₂-OC(=O)-,

wherein B represents a 1,4-phenyl group, and Z^1 represents the following structural formula:

[Formula 7]



wherein in the structural formula for Z¹, each asterisk * represents bonding to the C(=O) neighboring Z¹ and each wavy line represents bonding to the glycan bonding to N297 of Ab (N297 glycan) or bonding to a remodeled glycan.

[Claim 17]

The antibody-drug conjugate according to any one of claims 1 to 16, wherein the antibody is IgG1, IgG2 or IgG4.

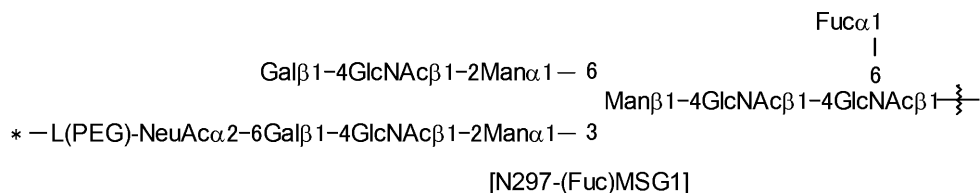
[Claim 18]

The antibody-drug conjugate according to any one of claims 1 to 17, wherein the N297 glycan is a remodeled glycan.

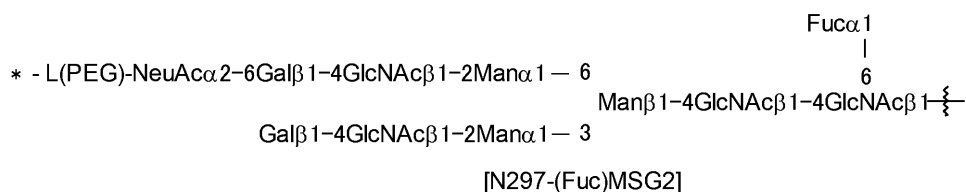
[Claim 19]

The antibody-drug conjugate according to any one of claims 1 to 18, wherein the N297 glycan is N297-(Fuc)MSG1, N297-(Fuc)MSG2, or a mixture thereof, or N297-(Fuc)SG, with N297-(Fuc)MSG1, N297-(Fuc)MSG2, and N297-(Fuc)SG having structures represented by the following formulas:

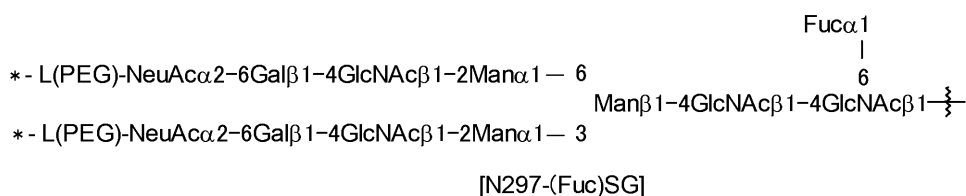
[Formula 10]



[Formula 11]



[Formula 12]



wherein the wavy line represents bonding to Asn297 of the antibody,

*-L(PEG)- in the N297 glycan represents *-(CH₂CH₂-O)ⁿ-CH₂CH₂-NH-, wherein n represents an integer of 2 to 5, the amino group at the right end is bound via an amide bond to the carboxylic acid at the 2-position of the sialic acid at the non-reducing terminal in each or either one of the 1-3 and 1-6 branched chains of the β-Man in the N297 glycan, and each asterisk * represents bonding to the nitrogen atom at the 1- or 3-position of the triazole ring in the individual structural formulas.

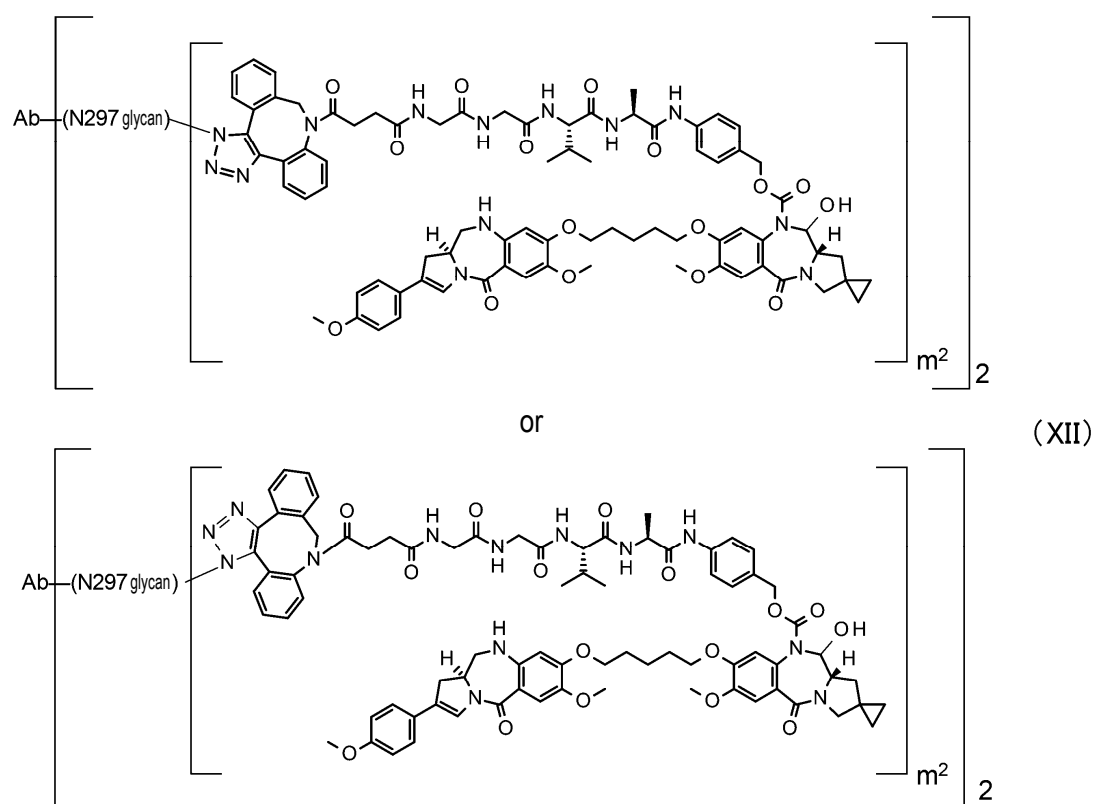
[Claim 20]

The antibody-drug conjugate according to claim 19, wherein n^5 represents 3.

[Claim 21]

An antibody-drug conjugate represented by the following formula (XII):

[Formula 13]



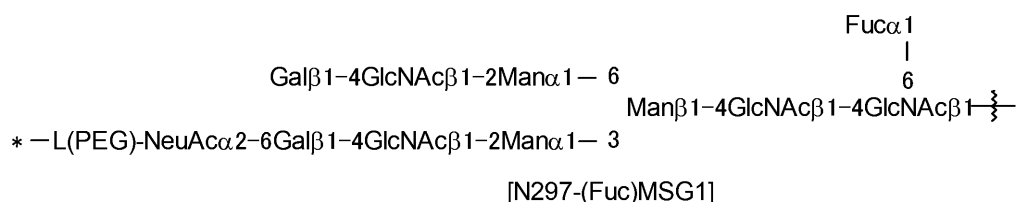
wherein, in each structural formula shown above,

m^2 represents an integer of 1 or 2,

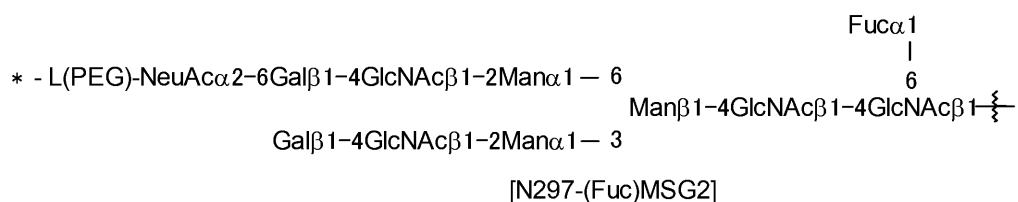
Ab represents an IgG antibody specifically binding to an amino acid sequence comprising the amino acid sequence shown in SEQ ID NO: 4 and having internalization ability that permits cellular uptake, or a functional fragment thereof,

the N297 glycan of Ab represents any one of N297-(Fuc)MSG1, N297-(Fuc)MSG2, and a mixture thereof, and N297-(Fuc)SG, with N297-(Fuc)MSG1, N297-(Fuc)MSG2, and N297-(Fuc)SG having structures represented by the following formulas,

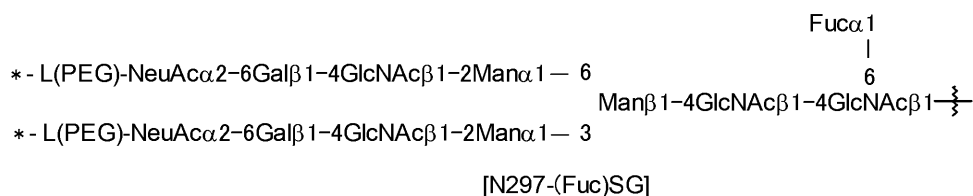
[Formula 14]



[Formula 15]



[Formula 16]



wherein each wavy line represents bonding to Asn297 (N297) of the antibody,

*-L(PEG)- in the N297 glycan represents *-(CH₂CH₂-O)₃-CH₂CH₂-NH-,

wherein

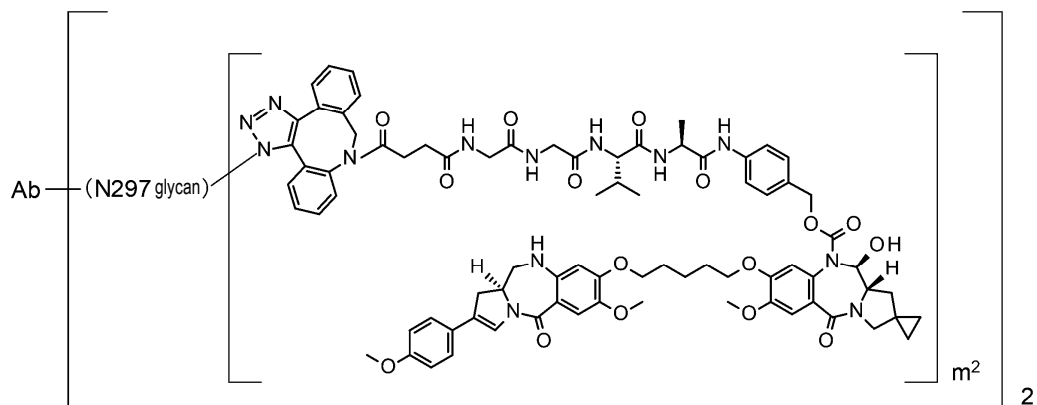
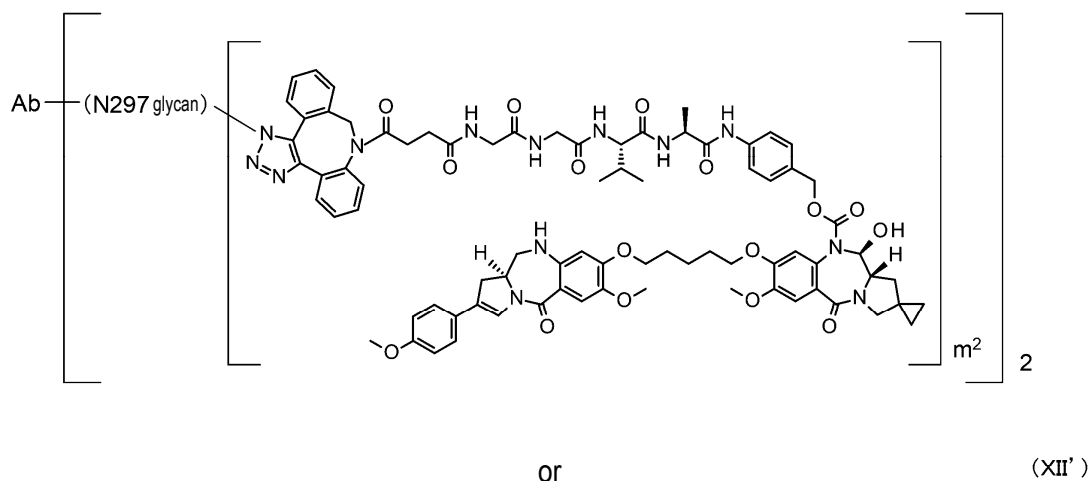
the amino group at the right end is bound via an amide bond to the carboxylic acid at the 2-position of

the sialic acid at the non-reducing terminal in each or either one of the 1-3 and 1-6 branched chains of the β -Man in the N297 glycan, and each asterisk * represents bonding to the nitrogen atom at the 1- or 3-position of the triazole ring in the corresponding structural formula.

[Claim 22]

The antibody-drug conjugate according to claim 21, wherein the compound represented by formula (XII) is represented by the following formula (XII'):

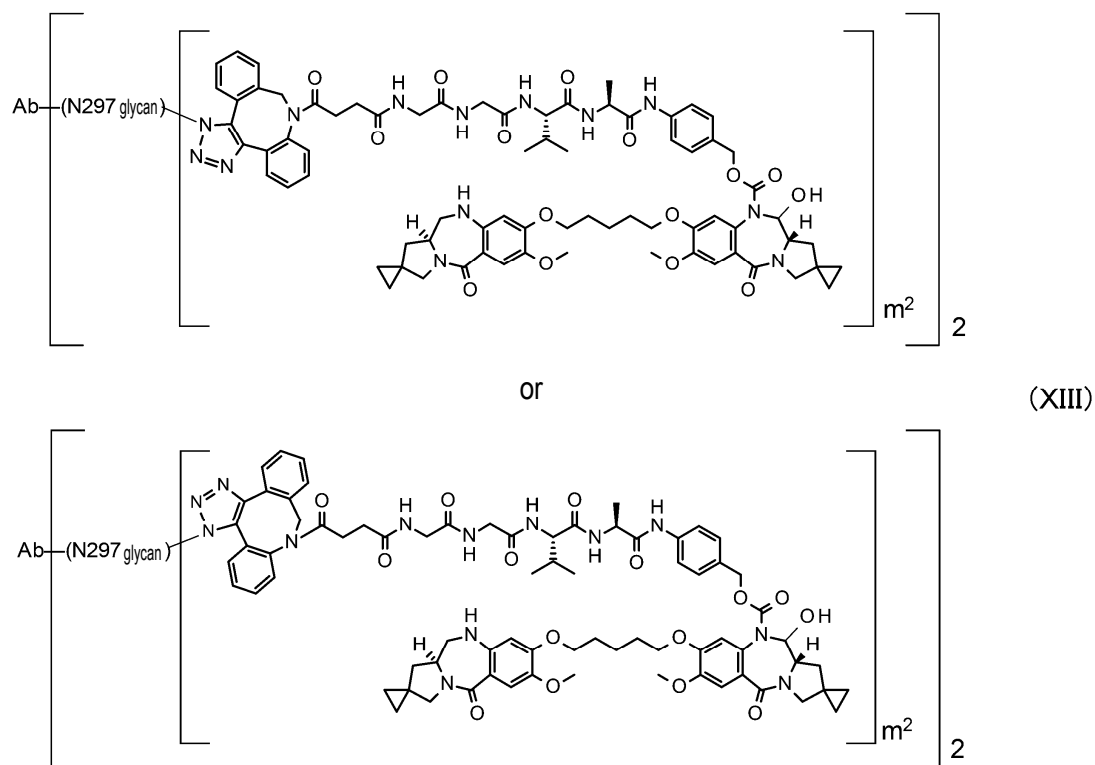
[Formula 17]



[Claim 23]

An antibody-drug conjugate represented by the following formula (XIII):

[Formula 18]



wherein, in each structural formula shown above,

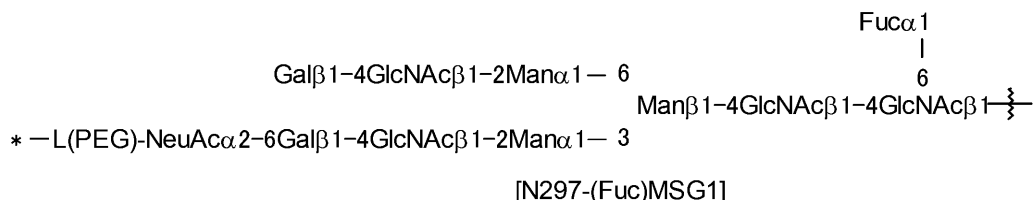
m^2 represents an integer of 1 or 2,

Ab represents an IgG antibody specifically binding to an amino acid sequence comprising the amino acid sequence shown in SEQ ID NO: 4 and having internalization ability that permits cellular uptake, or a functional fragment thereof, and

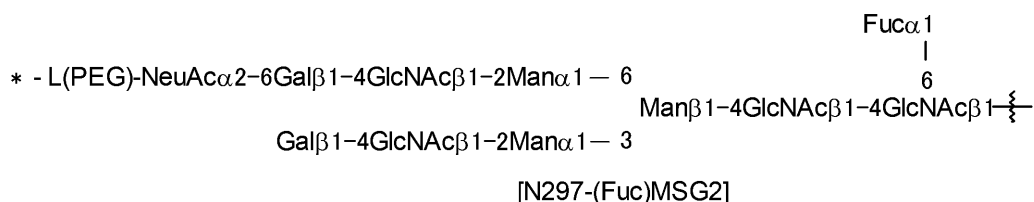
the N297 glycan of Ab represents any one of N297-(Fuc)MSG1, N297-(Fuc)MSG2, and a mixture thereof, and N297-(Fuc)SG, with N297-(Fuc)MSG1, N297-(Fuc)MSG2, and

N297-(Fuc)SG having structures represented by the following formulas,

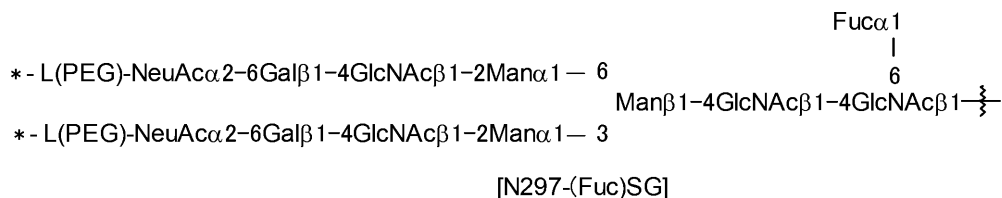
[Formula 19]



[Formula 20]



[Formula 21]



wherein each wavy line represents bonding to Asn297 (N297) of the antibody,

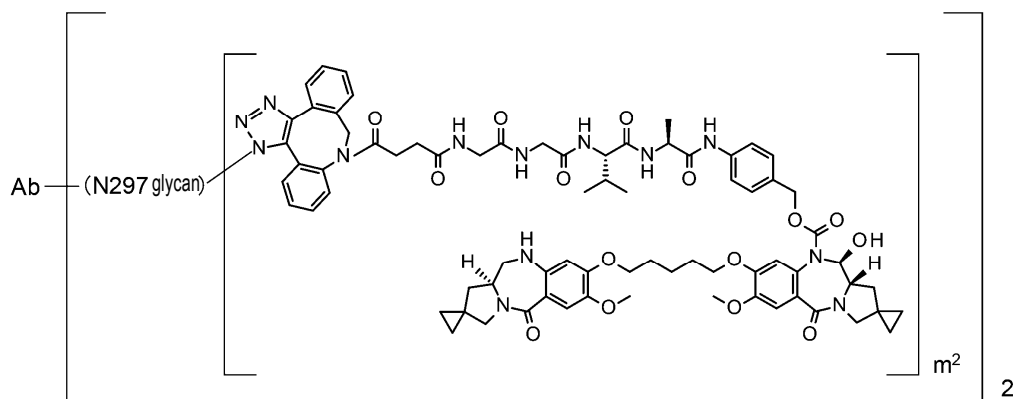
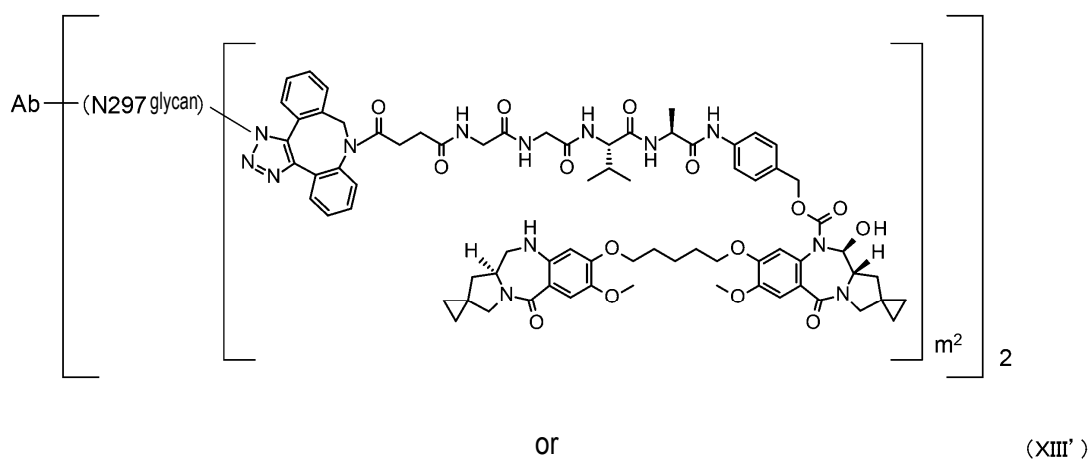
*-L(PEG)- in the N297 glycan represents *-(CH₂CH₂-O)₃-CH₂CH₂-NH-, wherein the amino group at the right end is bound via an amide bond to the carboxylic acid at the 2-position of the sialic acid at the non-reducing terminal in each or either one of the 1-3 and 1-6 branched chains of the β-Man in the N297 glycan, and each asterisk * represents bonding to the nitrogen atom at the

1- or 3-position of the triazole ring in the individual structural formulas.

[Claim 24]

The antibody-drug conjugate according to claim 23, wherein the compound represented by formula (XIII) is represented by the following formula (XIII'):

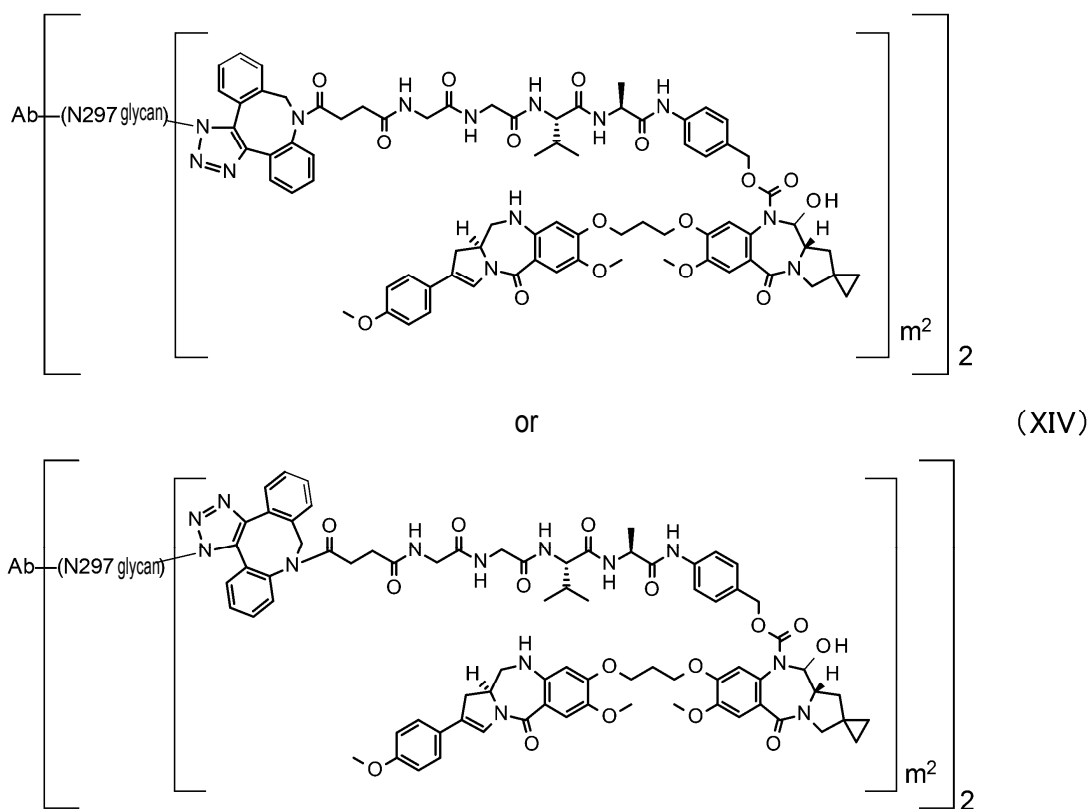
[Formula 22]



[Claim 25]

An antibody-drug conjugate represented by the following formula (XIV):

[Formula 23]



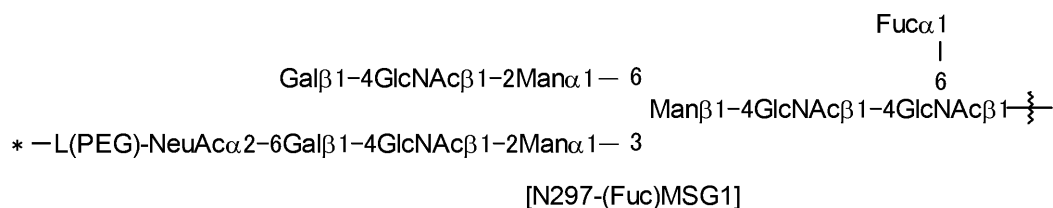
wherein, in each structural formula shown above,

m^2 represents an integer of 1 or 2,

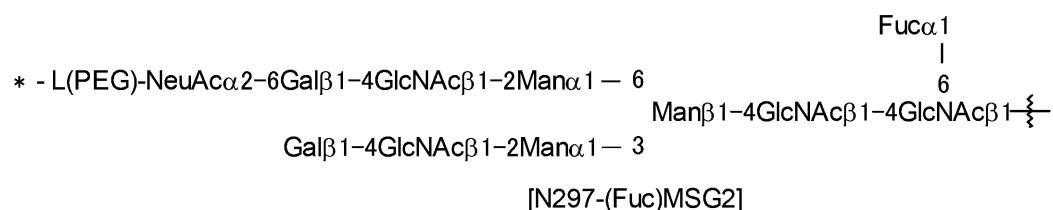
Ab represents an IgG antibody specifically binding to an amino acid sequence comprising the amino acid sequence shown in SEQ ID NO: 4 and having internalization ability that permits cellular uptake, or a functional fragment thereof, and

the N297 glycan of Ab represents any one of N297-(Fuc)MSG1, N297-(Fuc)MSG2, and a mixture thereof, and N297-(Fuc)SG, with N297-(Fuc)MSG1, N297-(Fuc)MSG2, and N297-(Fuc)SG having structures represented by the following formulas:

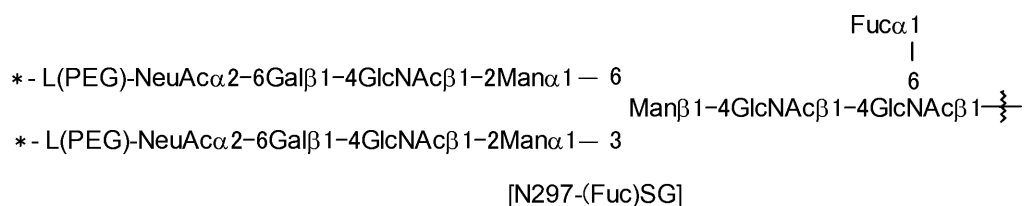
[Formula 24]



[Formula 25]



[Formula 26]



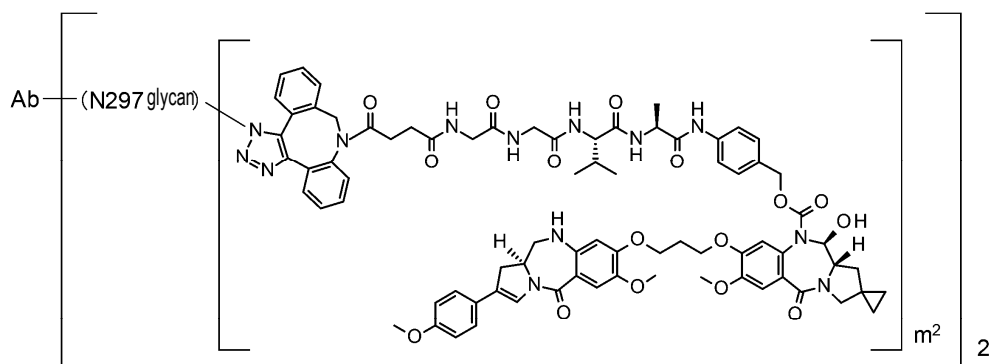
wherein each wavy line represents bonding to Asn297 (N297) of the antibody,

*-L(PEG)- in the N297 glycan represents *-(CH₂CH₂-O)₃-CH₂CH₂-NH-, wherein the amino group at the right end is bound via an amide bond to the carboxylic acid at the 2-position of the sialic acid at the non-reducing terminal in each or either one of the 1-3 and 1-6 branched chains of the β-Man in the N297 glycan, and each asterisk * represents bonding to the nitrogen atom at the 1- or 3-position of the triazole ring in the individual structural formulas.

[Claim 26]

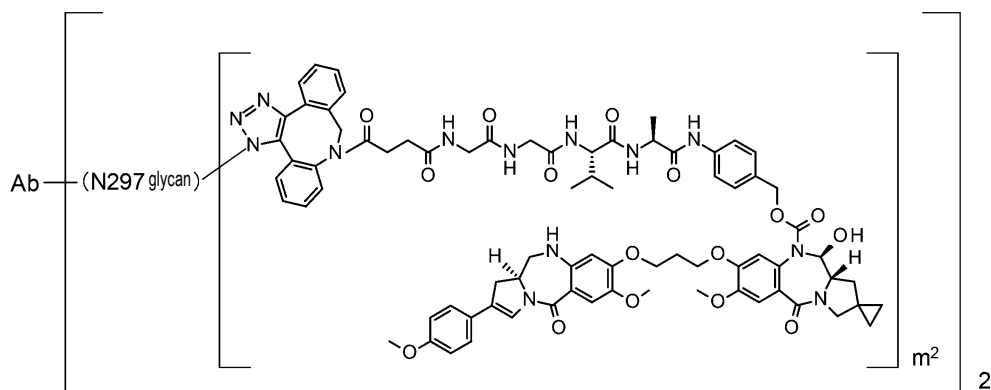
The antibody-drug conjugate according to claim 25,
wherein the compound represented by formula (XIV) is
represented by the following formula (XIV'):

[Formula 27]



or

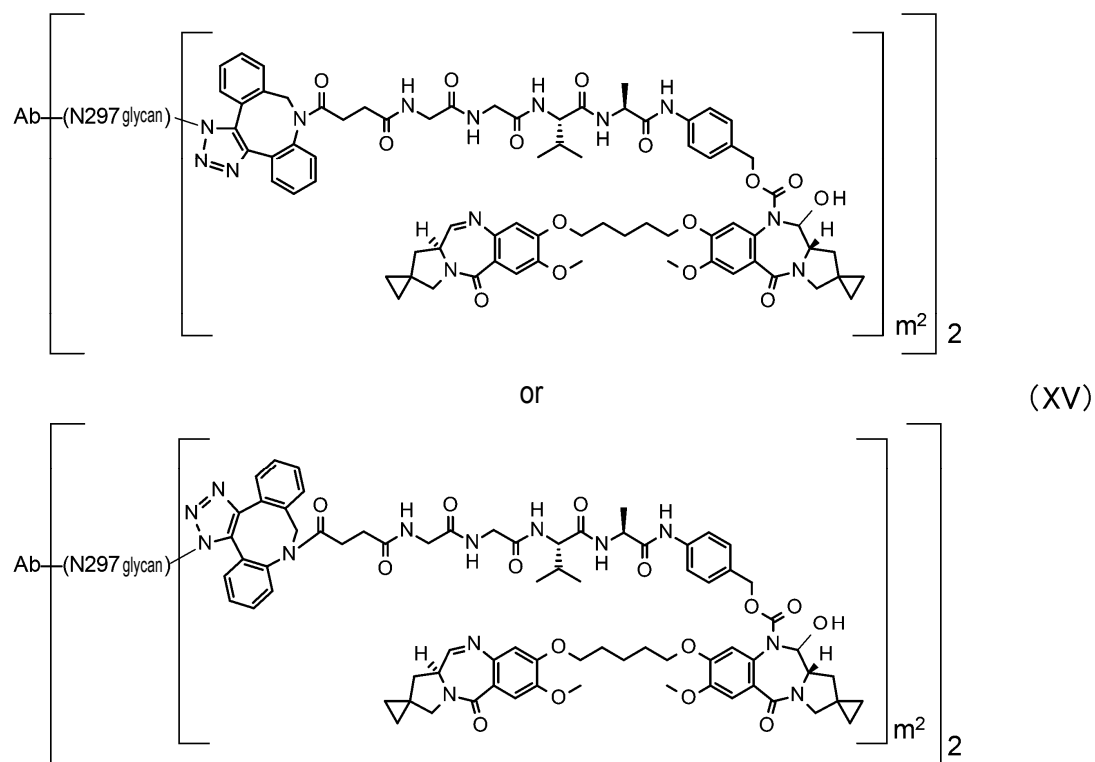
(XIV')



[Claim 27]

An antibody-drug conjugate represented by the following formula (XV):

[Formula 28]



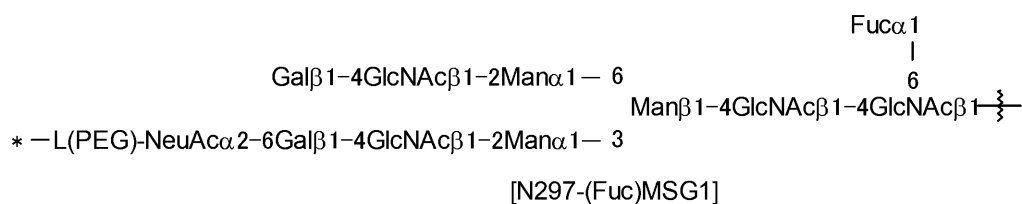
wherein, in each structural formula shown above,

m^2 represents an integer of 1 or 2,

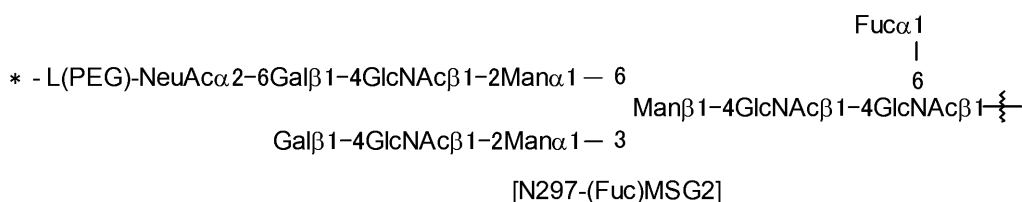
Ab represents an IgG antibody specifically binding to an amino acid sequence comprising the amino acid sequence shown in SEQ ID NO: 4 and having internalization ability that permits cellular uptake, or a functional fragment thereof, and

the N297 glycan of Ab represents any one of N297-(Fuc)MSG1, N297-(Fuc)MSG2, and a mixture thereof, and N297-(Fuc)SG, with N297-(Fuc)MSG1, N297-(Fuc)MSG2, and N297-(Fuc)SG having structures represented by the following formulas:

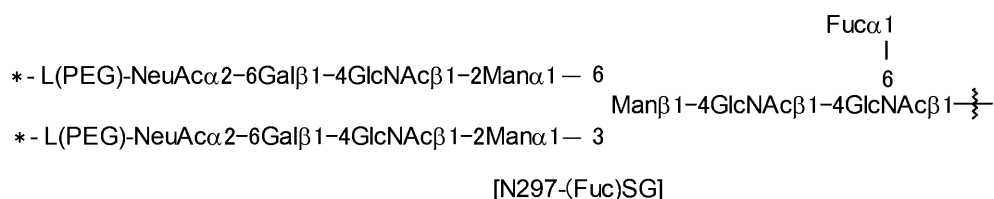
[Formula 29]



[Formula 30]



[Formula 31]



wherein each wavy line represents bonding to Asn297

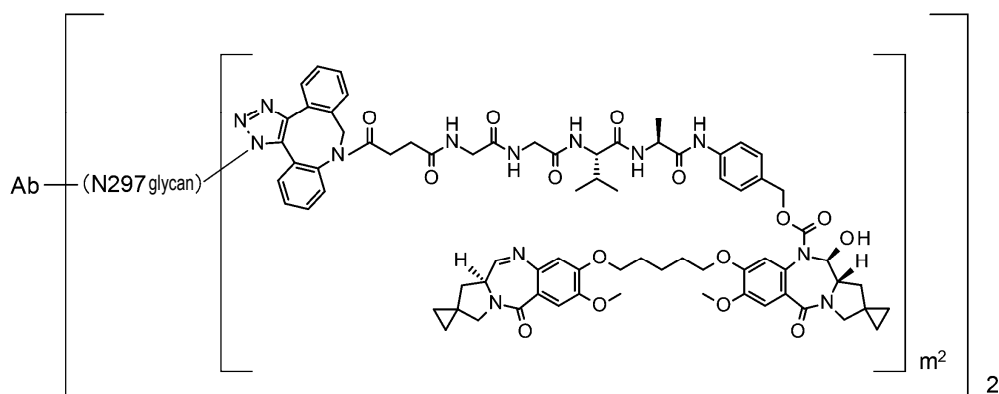
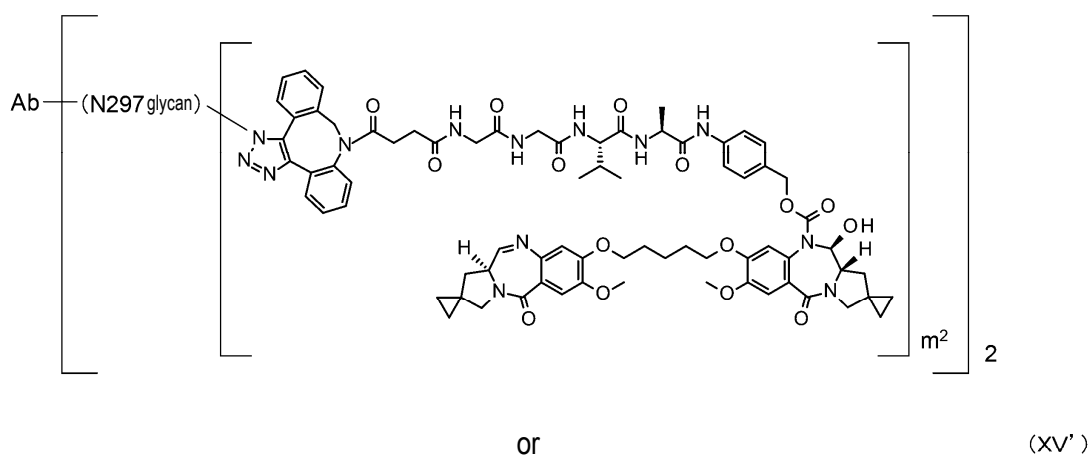
(N297) of the antibody,

*-L(PEG)- in the N297 glycan represents *-(CH₂CH₂-O)₃-CH₂CH₂-NH-, wherein the amino group at the right end is bound via an amide bond to the carboxylic acid at the 2-position of the sialic acid at the non-reducing terminal in each or either one of the 1-3 and 1-6 branched chains of the β-Man in the N297 glycan, and each asterisk * represents bonding to the nitrogen atom at the 1- or 3-position of the triazole ring in the individual structural formulas.

[Claim 28]

The antibody-drug conjugate according to claim 27, wherein the compound represented by formula (XV) is represented by the following formula (XV'):

[Formula 32]



[Claim 29]

The antibody-drug conjugate according to any one of claims 21 to 28, wherein the antibody or a functional fragment thereof comprises CDRL1, CDRL2 and CDRL3 and CDRH1, CDRH2 and CDRH3 selected from the group consisting of the following (1) to (4):

(1) CDRL1 consisting of the amino acid sequence shown in SEQ ID NO: 12, CDRL2 consisting of the amino

acid sequence shown in SEQ ID NO: 13 and CDRL3 consisting of the amino acid sequence shown in SEQ ID NO: 14 and CDRH1 consisting of the amino acid sequence shown in SEQ ID NO: 17, CDRH2 consisting of the amino acid sequence shown in SEQ ID NO: 18 and CDRH3 consisting of the amino acid sequence shown in SEQ ID NO: 19,

(2) CDRL1 consisting of the amino acid sequence shown in SEQ ID NO: 12, CDRL2 consisting of the amino acid sequence shown in SEQ ID NO: 13 and CDRL3 consisting of the amino acid sequence shown in SEQ ID NO: 14 and CDRH1 consisting of the amino acid sequence shown in SEQ ID NO: 17, CDRH2 consisting of the amino acid sequence shown in SEQ ID NO: 30 and CDRH3 consisting of the amino acid sequence shown in SEQ ID NO: 19,

(3) CDRL1 consisting of the amino acid sequence shown in SEQ ID NO: 12, CDRL2 consisting of the amino acid sequence shown in SEQ ID NO: 13 and CDRL3 consisting of the amino acid sequence shown in SEQ ID NO: 14 and CDRH1 consisting of the amino acid sequence shown in SEQ ID NO: 57, CDRH2 consisting of the amino acid sequence shown in SEQ ID NO: 58 and CDRH3 consisting of the amino acid sequence shown in SEQ ID NO: 59, and

(4) CDRL1 consisting of the amino acid sequence shown in SEQ ID NO: 12, CDRL2 consisting of the amino acid sequence shown in SEQ ID NO: 13 and CDRL3 consisting of the amino acid sequence shown in SEQ ID NO: 14 and CDRH1 consisting of the amino acid sequence shown in SEQ

ID NO: 62, CDRH2 consisting of the amino acid sequence shown in SEQ ID NO: 63 and CDRH3 consisting of the amino acid sequence shown in SEQ ID NO: 64.

[Claim 30]

The antibody-drug conjugate according to any one of claims 21 to 29, wherein the antibody or a functional fragment thereof comprises any one of the following (1) to (6):

(1) a light chain variable region consisting of the amino acid sequence shown in SEQ ID NO: 33 and a heavy chain variable region consisting of the amino acid sequence shown in SEQ ID NO: 41,

(2) a light chain variable region consisting of the amino acid sequence shown in SEQ ID NO: 33 and a heavy chain variable region consisting of the amino acid sequence shown in SEQ ID NO: 45,

(3) a light chain variable region consisting of the amino acid sequence shown in SEQ ID NO: 37 and a heavy chain variable region consisting of the amino acid sequence shown in SEQ ID NO: 45,

(4) a light chain variable region consisting of the amino acid sequence shown in SEQ ID NO: 33 and a heavy chain variable region consisting of the amino acid sequence shown in SEQ ID NO: 49,

(5) a light chain variable region consisting of the amino acid sequence shown in SEQ ID NO: 33 and a heavy

chain variable region consisting of the amino acid sequence shown in SEQ ID NO: 55 or

(6) a light chain variable region consisting of the amino acid sequence shown in SEQ ID NO: 33 and a heavy chain variable region consisting of the amino acid sequence shown in SEQ ID NO: 60.

[Claim 31]

The antibody-drug conjugate according to any one of claims 21 to 30, wherein the antibody or a functional fragment thereof comprises any one of the following (1) to (7):

(1) a light chain consisting of the amino acid sequence at positions 21 to 233 in SEQ ID NO: 31 and a heavy chain consisting of the amino acid sequence at positions 20 to 471 in SEQ ID NO: 39,

(2) a light chain consisting of the amino acid sequence at positions 21 to 233 in SEQ ID NO: 31 and a heavy chain consisting of the amino acid sequence at positions 20 to 471 in SEQ ID NO: 43,

(3) a light chain consisting of the amino acid sequence at positions 21 to 233 in SEQ ID NO: 35 and a heavy chain consisting of the amino acid sequence at positions 20 to 471 in SEQ ID NO: 43,

(4) a light chain consisting of the amino acid sequence at positions 21 to 233 in SEQ ID NO: 31 and a heavy chain consisting of the amino acid sequence at positions 20 to 471 in SEQ ID NO: 47,

(5) a light chain consisting of the amino acid sequence at positions 21 to 233 in SEQ ID NO: 31 and a heavy chain consisting of the amino acid sequence at positions 20 to 471 in SEQ ID NO: 65,

(6) a light chain consisting of the amino acid sequence at positions 21 to 233 in SEQ ID NO: 31 and a heavy chain consisting of the amino acid sequence at positions 20 to 471 in SEQ ID NO: 67 and

(7) a light chain consisting of the amino acid sequence at positions 21 to 233 in SEQ ID NO: 31 and a heavy chain consisting of the amino acid sequence at positions 20 to 471 in SEQ ID NO: 69.

[Claim 32]

The antibody-drug conjugate according to claim 31, wherein the antibody or a functional fragment thereof comprises a light chain consisting of the amino acid sequence at positions 21 to 233 in SEQ ID NO: 31 and a heavy chain consisting of the amino acid sequence at positions 20 to 471 in SEQ ID NO: 39.

[Claim 33]

The antibody-drug conjugate according to claim 31, wherein the antibody or a functional fragment thereof comprises a light chain consisting of the amino acid sequence at positions 21 to 233 in SEQ ID NO: 31 and a heavy chain consisting of the amino acid sequence at positions 20 to 471 in SEQ ID NO: 43.

[Claim 34]

The antibody-drug conjugate according to claim 31, wherein the antibody or a functional fragment thereof comprises a light chain consisting of the amino acid sequence at positions 21 to 233 in SEQ ID NO: 35 and a heavy chain consisting of the amino acid sequence at positions 20 to 471 in SEQ ID NO: 43.

[Claim 35]

The antibody-drug conjugate according to claim 31, wherein the antibody or a functional fragment thereof comprises a light chain consisting of the amino acid sequence at positions 21 to 233 in SEQ ID NO: 31 and a heavy chain consisting of the amino acid sequence at positions 20 to 471 in SEQ ID NO: 47.

[Claim 36]

The antibody-drug conjugate according to claim 31, wherein the antibody or a functional fragment thereof comprises a light chain consisting of the amino acid sequence at positions 21 to 233 in SEQ ID NO: 31 and a heavy chain consisting of the amino acid sequence at positions 20 to 471 in SEQ ID NO: 65.

[Claim 37]

The antibody-drug conjugate according to claim 31, wherein the antibody or a functional fragment thereof comprises a light chain consisting of the amino acid sequence at positions 21 to 233 in SEQ ID NO: 31 and a

heavy chain consisting of the amino acid sequence at positions 20 to 471 in SEQ ID NO: 67.

[Claim 38]

The antibody-drug conjugate according to claim 31, wherein the antibody or a functional fragment thereof comprises a light chain consisting of the amino acid sequence at positions 21 to 233 in SEQ ID NO: 31 and a heavy chain consisting of the amino acid sequence at positions 20 to 471 in SEQ ID NO: 69.

[Claim 39]

The antibody-drug conjugate according to any one of claims 1 to 38, wherein the average number of conjugated drug molecules per antibody molecule in the antibody-drug conjugate is 1 to 3.

[Claim 40]

The antibody-drug conjugate according to any one of claims 1 to 38, wherein the average number of conjugated drug molecules per antibody molecule in the antibody-drug conjugate is 3 to 5.

[Claim 41]

The antibody-drug conjugate according to any one of claims 1 to 40, wherein the antibody contains a heavy chain having one or two or more modifications selected from the group consisting of N-linked glycosylation, O-linked glycosylation, N-terminal processing, C-terminal processing, deamidation, isomerization of aspartic acid, oxidation of methionine, addition of a methionine residue

to the N-terminus, amidation of a proline residue, and a deletion of one or two amino acids from the carboxyl terminus.

[Claim 42]

The antibody-drug conjugate according to any one of claims 1 to 41, wherein the lysine residue at the carboxyl terminus of a heavy chain is deleted.

[Claim 43]

A method for producing a glycan-remodeled antibody, the method comprising the steps of:

i) producing an IgG antibody specifically binding to an amino acid sequence comprising the amino acid sequence shown in SEQ ID NO: 4 and having internalization ability that permits cellular uptake, or a functional fragment thereof,

ii) treating the antibody obtained in step i) with hydrolase to produce a (Fuc α 1,6)GlcNAc-antibody; and

iii)-1 reacting the (Fuc α 1,6)GlcNAc-antibody and a glycan donor molecule in the presence of a transglycosidase, the glycan donor molecule obtained by introducing a PEG linker having an azide group to the carbonyl group of carboxylic acid at the 2-position of a sialic acid in MSG (9) or SG (10) and oxazolinating the reducing terminal, or

iii)-2 reacting the (Fuc α 1,6)GlcNAc-antibody and a glycan donor molecule in the presence of a transglycosidase, the glycan donor molecule obtained by

introducing a PEG linker having an azide group to the carbonyl group of carboxylic acid at the 2-position of a sialic acid in (MSG-)Asn or (SG-)Asn with an α -amino group optionally protected and to the carbonyl group of carboxylic acid in the Asn, causing action of hydrolase, and then oxazolinating the reducing terminal.

[Claim 44]

A method for producing an antibody-drug conjugate according to any one of claims 1 to 42, comprising the step of reacting the glycan-remodeled antibody obtained by the method according to claim 43 and a drug linker.

[Claim 45]

The antibody-drug conjugate according to any one of claim 1 to 42, produced by the method according to claim 44.

[Claim 46]

An antibody or a functional fragment thereof, comprising a light chain variable region, which contains CDRL1 consisting of the amino acid sequence shown in SEQ ID NO: 12, CDRL2 consisting of the amino acid sequence shown in SEQ ID NO: 13 and CDRL3 consisting of the amino acid sequence shown in SEQ ID NO: 14, and a heavy chain variable region, which contains CDRH1 consisting of the amino acid sequence shown in SEQ ID NO: 57, CDRH2 consisting of the amino acid sequence shown in SEQ ID NO: 58 and CDRH3 consisting of the amino acid sequence shown in SEQ ID NO: 59.

[Claim 47]

An antibody or a functional fragment thereof, comprising a light chain variable region, which contains CDRL1 consisting of the amino acid sequence shown in SEQ ID NO: 12, CDRL2 consisting of the amino acid sequence shown in SEQ ID NO: 13 and CDRL3 consisting of the amino acid sequence shown in SEQ ID NO: 14; and a heavy chain variable region, which contains CDRH1 consisting of the amino acid sequence shown in SEQ ID NO: 62, CDRH2 consisting of the amino acid sequence shown in SEQ ID NO: 63 and CDRH3 consisting of the amino acid sequence shown in SEQ ID NO: 64.

[Claim 48]

The antibody or a functional fragment thereof according to claim 46, comprising a light chain variable region consisting of the amino acid sequence shown in SEQ ID NO: 33 and a heavy chain variable region consisting of the amino acid sequence shown in SEQ ID NO: 55.

[Claim 49]

The antibody or a functional fragment thereof according to claim 47, comprising a light chain variable region consisting of the amino acid sequence shown in SEQ ID NO: 33 and a heavy chain variable region consisting of the amino acid sequence shown in SEQ ID NO: 60.

[Claim 50]

The antibody or a functional fragment thereof according to claim 46 or 48, having a light chain

consisting of the amino acid sequence at positions 21 to 233 in SEQ ID NO: 31 and a heavy chain consisting of the amino acid sequence at positions 20 to 471 in SEQ ID NO: 67.

[Claim 51]

The antibody or a functional fragment thereof according to claim 47 or 49, having a light chain consisting of the amino acid sequence at positions 21 to 233 in SEQ ID NO: 31 and a heavy chain consisting of the amino acid sequence at positions 20 to 471 in SEQ ID NO: 69.

[Claim 52]

An antibody or a functional fragment thereof having a light chain consisting of the amino acid sequence at positions 21 to 233 in SEQ ID NO: 31 and a heavy chain consisting of the amino acid sequence at positions 20 to 471 in SEQ ID NO: 65.

[Claim 53]

A polynucleotide encoding the antibody according to any one of claims 46 to 52.

[Claim 54]

An expression vector containing the polynucleotide according to claim 53.

[Claim 55]

A host cell transformed with the expression vector according to claim 54.

[Claim 56]

A method for producing the antibody or a functional fragment thereof according to any one of claims 46 to 52, comprising a step of culturing the host cell according to claim 55 and collecting the targeted antibody from the culture obtained from the step of culturing.

[Claim 57]

An antibody or a functional fragment thereof, obtained by the method according to claim 56.

[Claim 58]

A pharmaceutical composition containing the antibody-drug conjugate according to any one of claims 1 to 42 and 45 or an antibody or a functional fragment thereof according to any one of claims 46 to 52 and 57.

[Claim 59]

The pharmaceutical composition according to claim 58, which is an antitumor drug.

[Claim 60]

The pharmaceutical composition according to claim 59, wherein the tumor is a tumor expressing CDH6.

[Claim 61]

The pharmaceutical composition according to claim 60, wherein the tumor is renal cell carcinoma, renal clear cell carcinoma, papillary renal cell carcinoma, ovarian cancer, ovarian serous adenocarcinoma, thyroid cancer, bile duct cancer, lung cancer, small-cell lung

cancer, non-small cell lung cancer, glioblastoma, mesothelioma, uterine cancer, pancreatic cancer, Wilms' tumor or neuroblastoma.

[Claim 62]

Use of the antibody-drug conjugate according to any one of claims 1 to 42 and 45, the antibody or a functional fragment thereof according to any one of claims 46 to 52 and 57 or the pharmaceutical composition according to any one of claims 58 to 61, in the manufacture of a medicament for treating a tumor.

[Claim 63]

The use according to claim 62, wherein the tumor is a tumor having CDH6 expressed therein.

[Claim 64]

The use according to claim 62 or 63, wherein the tumor is renal cell carcinoma, renal clear cell carcinoma, papillary renal cell carcinoma, ovarian cancer, ovarian serous adenocarcinoma, thyroid cancer, bile duct cancer, lung cancer, small-cell lung cancer, non-small cell lung cancer, glioblastoma, mesothelioma, uterine cancer, pancreatic cancer, Wilms' tumor or neuroblastoma.

[Claim 65]

The use according to any one of claims 62 to 64, wherein the medicament is for administering the antibody-drug conjugate according to any one of claims 1 to 42 and 45, the antibody or a functional fragment thereof

according to any one of claims 46 to 52 and 57, or the pharmaceutical composition according to any one of claims 58 to 61 to an individual simultaneously, separately or continuously with at least one antitumor drug.